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SURGICAL TREATMENT OF OBESITY

A clinical, biochemical and psychological evaluation
of obese patients before and after
weight reduction by gastroplasty



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Abstract The gastroplasty procedure was evaluated as a means to achieve weight reduction in 24 morbidly obese patients. The patients were extensively studied before and repeatedly after surgery. One patient suffered a lethal pulmonary embolus immediately after surgery. The weight reduction showed great interindividual variation (1-71 kg, 18 months after surgery) and was unsatisfactory (< 20%) in 1/3 of the patients. Psychologically, signs of depression increased after weight reduction and depressive reactions were more prevalent in patients, who lost most weight. The psychological profile recorded prior to surgery could differentiate successful from unsuccessful patients with regard to weight reduction. After weight reduction, the metabolic disturbances found prior to surgery improved drastically. Cardiovascular risk factors such as hyperlipoproteinemia, hyperinsulinemia and glucose intolerance were eliminated or reduced. Gastric acid secretion decreased considerably and no morphologic changes in the gastric mucosa were seen postoperatively. Comparison of data obtained before and after weight reduction gave no indication that any of the biochemical aberrations noted (especially adipose tissue lipoprotein lipase activity and adipocyte heat production) would represent a primary etiological factor for obesity in these patients. Although comparatively simple and free from metabolic side effects, the gastroplasty procedure should be used restrictively until the variability in weight reduction can be controlled.			
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A clinical, biochemical and psychological evaluation of obese
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by

Sven-Åke Olsson

Lund 1984

To Babs, Marie och Malin

This thesis is based on the following papers, which in the text will be referred to by their Roman numerals.

- I Olsson, S-Å., Nilsson-Ehle, P., Petterson, B-G., Sörbris, R.
Gastroplasty as a treatment for massive obesity - a clinical and biochemical evaluation. Scandinavian Journal of Gastroenterology (in press).
- II Olsson, S-Å., Nilsson-Ehle, P., Petterson, B-G., Sörbris, R.
Effects of weight reduction after gastroplasty on glucose and lipid metabolism. American Journal of Clinical Nutrition (in press).
- III Olsson, S-Å., Monti, M., Sörbris, R., Nilsson-Ehle, P.
Adipocyte heat production before and after weight reduction by gastroplasty. Submitted.
- IV Rydén, O., Olsson, S-Å., Danielsson, A., Nilsson-Ehle, P.
Weight loss after gastroplasty: Psychological sequelae in relation to clinical and metabolic observations. (Submitted)
- V Olsson, S-Å., Rydén, O., Danielsson, A., Nilsson-Ehle, P.
Weight reduction after gastroplasty - The predictive value of surgical, metabolic and psychological variables. International Journal of Obesity 1984: 8, 245-258.

Abbreviations used: HDL, High Density Lipoprotein; HL, Hepatic lipase; LBM, Lean body mass; LDL, Low Density Lipoprotein; LPL, Lipoprotein lipase; MCT; Meta-Contrast Technique; RFT, Rod and Frame Test; T4, thyroxine; T3, triiodothyronine; rT3, reversed triiodothyronine; VLDL, Very Low Density Lipoprotein.



*Leave gourmandizing. Know the grave doth gape
For thee thrice wider than for other men.*

William Shakespeare
HENRY IV, part II; V, v, 54-55.

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1 BACKGROUND

1.1 Definition

The term obesity is derived from ob (over) and edere (to eat), implicating that obesity is caused by overeating. Adiposity is defined as an excess of adipose tissue and may thus exist in a normal weight individual. Although normal weight is badly defined (1, 2), overweight generally indicates a body weight exceeding the "ideal weight" by more than 10 %. Similarly, obesity usually refers to a body weight 20 % over the "ideal". For more pronounced obesity, which may lead to metabolic complications and cause social and psychological problems, the term morbid obesity has been used. However, no generally accepted definition for the term has yet been developed, although numerous formulas (3) have been applied to quantitate the excessive adipose tissue in obese individuals. In the United States the Body Mass Index* is widely used especially for scientific purposes, whereas Broca's index** is more common in Europe; this later formula can easily be understood also by laymen. In clinical practice, morbid obesity has been reserved for patients with at least 50 % overweight (Broca's index > 1.5; Body Mass index > 37); in this group the mortality rate is clearly elevated.

$$* \text{ BMI} = \frac{\text{body weight (kg)}}{\text{height}^2 \text{ (m)}}$$

$$** \text{ BI} = \frac{\text{body weight (kg)}}{\text{height (cm)} - 100}$$



1.2 Prevalence

Among adults in the USA the prevalence of obesity varies with age and sex (4). In the third decade about ten per cent of the women are overweight; this number increases continuously to 45 % in the fifth decade. The corresponding figures for men are 20 % and 29 %, respectively. Approximately 15 % of the male and 25 % of the female population between 21 and 74 years of age in the United States can be classified as obese, i.e. their body weight exceeds the ideal by 20 % (5).

Data regarding the prevalence of morbid obesity in the USA (3, 6, 7) indicate that among men aged 21 - 74 years 4.9 % (2.8 millions) weigh more than 110 kg. An even larger proportion (7.2 %, 4.5 millions) of the women of the same age exceed 110 kg. However, less than 0.1 % (approximately 60 000) of the women weighed more than 136 kg. Despite lack of accurate figures, it is reasonable to believe that the problem is of almost the same magnitude in Sweden.

1.3 Etiology

The etiologic mechanisms behind obesity are still unknown. Many theories have been proposed (8, 9), indicating a multifactorial background. Only rarely is obesity caused by endocrine disorders (e. g. hypothyreoidism, Cushing's disease).

Whatever the cause, obesity is the result of a positive energy balance. This must be due to an increased energy input, to a decreased energy output or to a combination of these two possibilities. Since the efficiency of food absorption is almost 100 % in individuals without bowel disease (10), the input is, for practical purposes, equal to the amount of food ingested. Most studies of human food intake for practical reasons include normal weight and already obese individuals. Such studies have not revealed any important differences between obese and normal weight subjects. On the contrary studies among obese children (11, 12) have demonstrated that these may eat less than do normal weight children. However, the food intake during the phase when a person becomes obese remains to be studied. There is no doubt, however, that several morbidly obese subjects have a grossly pathological food intake behaviour (13). Some overeat and a great number do not eat because they are hungry; nor do they usually eat because food is very tasty. They are in fact true addicts and many theories including genetic predisposition and environmental influence have been proposed as explanations for the pathologic food intake, but a satisfactory answer to this problem remains to be found (9).

Energy output can be divided into three parts; physical work, "internal activity" (e. g. the energy necessary for fundamental biochemical reactions such as regulatory systems in the cell and for the maintenance of electric and osmotic gradients) and heat lost by the human body. Differences in the energy output may well exist; for example, obese individuals tend to be physically less

active than lean subjects (11, 12, 14) and some data (15, 16) suggest decreased "internal activities" or enhanced metabolic efficiency in obesity. Some of these findings may represent an adaptation to overweight or to metabolic disturbances following the obese state rather than causes of obesity. On the other hand some reports (17, 18) demonstrate that "spontaneously" obese subjects maintain their body weight surprisingly constant on significantly lower energy than do normal weight individuals made overweight by overfeeding. However, it should be born in mind that the previous methods to reveal differences in energy input (19) and output in order to detect the minor differences, which might lead to obesity, did not reach desirable accuracy. The introduction of new techniques, e.g. microcalorimetry (20) and the refinement of older ones, such as whole body calorimetry, (21) for measurements of energy expenditure, may in the future help us to further trace even minor differences in energy output important for the development of obesity.

A number of metabolic disturbances have been described in obesity (see below), but these seem to be consequences rather than causes of obesity. However, Schwartz and Brunzell (22) have reported that the activity of lipoprotein lipase in adipose tissue remained elevated in previously obese subjects, implicating that abnormalities in this enzyme system may play a role in the development of obesity. Other studies (23, 24) have not been able to verify this hypothesis. It should also be emphasized, that this enzyme system is only involved in the transport of energy from one compartment (plasma) to another (adipocyte lipid depot), a phenomenon, that in itself would not primarily lead to an increased body weight. An increased activity of this enzyme, promoting an accelerated uptake of plasma triglyceride into adipose tissue may of course lead to alterations in other variables influencing energy balance, i.e. an increased energy

input (food intake) or a decreased energy output (as internal activity or as heat). At present there are no data supporting these speculations.

1.4 Consequences of obesity

Obesity is considered to be a major health problem in the Western world (25, 26, 27, 28) and is associated with increased morbidity and mortality (29). Most data published in the United States are derived from insurance statistics and figures may underestimate the issue, as an insured population is selected among better risks. Among morbidly obese men (average weight 143.5 kg) the mortality in comparison with normal males showed a twelve fold increase for the age group between 25 - 34 years and a six fold increase in ages 35 - 44 (29).

The classical view (30, 31, 32) that an increased frequency of metabolic disturbances followed especially hypertrophic (increased adipocyte size) obesity compared to the hyperplastic (increased adipocyte number) type of obesity has lately been deemphasized, since most really obese individuals have a combined obesity (increased number and size of adipocytes). Recently it has been documented (33) that the distribution of the adipose tissue is critical for the morbidity and mortality in cardiovascular diseases. Accumulation of abdominal fat is considered to predispose for metabolic complications. For example, in equally obese subjects, it was demonstrated that the incidence of cardiovascular diseases increases eleven fold between the lowest and the highest decile for waist - hip ratio.

1.4.1 Associated disorders

Mortality and morbidity in cardio-cerebro-vascular disorders are higher among the obese (25, 34). In a Swedish report a correlation between hypertension and obesity has been found (35). It appears that obesity causes commonly occurring diseases to begin at an earlier age and to progress more rapidly. In moderate obesity, the increased risk seems mainly to be due to alterations in endocrine pancreatic function, adipose tissue metabolism, and glucose and lipid transport. Massive obesity, in addition, represents an independent risk factor (36). Considerable evidence exists that gallbladder disease is associated with obesity (37, 38) and surgery in this group of patients may also create increased mortality figures. Moreover, obese subjects develop diabetes mellitus more often than do lean persons (39) and death from diabetes is almost four times more common in obese individuals. Some authors (40) have also reported a higher incidence of endometrial carcinoma and menstrual disturbances (41) in obese women. However, another study (29) has showed that neoplasms were less frequent among morbidly obese men, probably because of many deaths at a relatively early age.

Pulmonary function may also undergo severe alterations in the morbidly obese patients (42) and hypoventilation may cause the so called Pickwickian syndrome (43).

1.4.2 Metabolic disturbances

Obesity is followed by a number of metabolic alterations and some of them are well known as cardiovascular risk factors representing the biochemical base for the increased morbidity and mortality in cardiovascular diseases. An increase in adipose tissue mass and enlargement of fat cells followed by augmented insulin resistance increases the demand for insulin from the pancreas,

which leads to hyperinsulinemia (24, 32, 44, 45, 46). In spite of the increased serum levels of insulin, the plasma levels of glucose are generally elevated, reflecting the increased insulin resistance in the peripheral tissues; this may eventually result in a failure of the pancreas to further increase the production of insulin and lead to diabetes. Also the regulation of glucagon secretion is disturbed (24, 47, 48, 49).

The plasma lipoprotein pattern often demonstrates HDL levels in the lower reference range and LDL concentrations in the upper reference range. Serum triglycerides are frequently elevated, which may be secondary to both endocrine and metabolic effects of the obese state (24). Thus, the increased insulin production may stimulate the liver to produce VLDL, probably by enhancing lipogenesis and by preventing hepatic triglyceride break down. The lipoprotein lipase activity is also disturbed, possibly as a consequence of glucose intolerance (50, 51), a fact which results in elevated serum levels of triglycerides. Cellular activity of lipoprotein lipase in adipose tissue is increased (24, 50, 51, 52, 53, 54, 55) and does not show the normal response to glucose intake (50). These alterations seem to ameliorate on weight reduction (56, 57), e. g. they seem to be consequences rather than causes of obesity. Some authors (22) however, have reported (as discussed more in detail above), that lipoprotein lipase activity in adipose tissue remains elevated in previously obese individuals, implicating that these abnormalities have a role in the development of obesity. The abnormal adipocyte metabolism in obese individuals can also be monitored using microcalorimetry (58) to measure total metabolic activity in the adipocyte. Adipocytes from obese individuals have a significantly lower metabolic activity than those from lean individuals (58). It is not yet clear whether the reduced adipocyte heat production is a primary factor contributing to the development of obesity or a phenomenon secondary to the obese state. There are data indicating (58) that

serum levels of insulin may be a determinant of adipocyte heat production, but it still remains unclear whether thyroid function regulates adipocyte heat production.

1.4.3 Psychological disturbances

In spite of numerous investigations and many theories no personality trait has been found to be characteristic for all, or even most, obese subjects. Psychological differences between obese subjects and normal controls have been reported although they have been difficult to replicate; the same is true for psychiatric abnormalities. The question of the hen or the egg is valid for psychological as well as for somatic findings; it is difficult to conclude whether they are causes of or caused by the obese state. Leon (59) and Webb (60) evaluated patients prior to jejuno-ileal bypass surgery and found only mild personality disorders. Other investigators have reported varying degrees of depression, neurosis and personality disorders but also quite normal psychological findings in obese patients (61, 62, 63). Positive psychological changes have been reported following intestinal and gastric bypass surgery (64, 65, 66, 67, 68) suggesting that psychological problems, noted in many morbidly obese persons prior to weight loss, occur as a consequence of their obesity. In contrast some investigators report postoperative psychological crises (depression, anxiety and marital problems) in as much as 20 - 60 % of the patients (69, 70, 71, 72, 73). These diverging reports can, no doubt, be attributed to differences in criteria and methodology used in the evaluation and, in particular, what proportion of the original sample of patients is available for reinvestigation. We have located no previous study which deals with the psychological aspects of the treatment of morbid obesity by gastroplasty and no attempt seems to have been made to evaluate possible psychological sequelae in relation to clinical and metabolic observations following this treatment.

1.5 Treatment of obesity

The etiology and pathogenesis of obesity is still speculative, which is reflected by the wide variety of therapeutic approaches to morbid obesity. The large number of moderately obese individuals is attracting a great commercial interest and the patients are often promised an unrealistic weight loss, which, if it is not achieved, is discouraging. Overweight as such is not a major indication for treatment. Instead, serious therapeutic measures should be started when complications (e.g. hypertension, metabolic disturbances or pain in weight bearing joints) arise as a consequence of the obese state. Therefore, a treatment program giving moderate or disappointing weight reduction must not necessarily be regarded as a failure; if risk factors are eliminated or reduced, the overall result is clearly beneficial for the patient. In some cases even a transient weight reduction may improve the patient's social situation.

Conservative methods to treat obesity are generally inexpensive, but the long term result is discouraging. In contrast, surgical treatment is often expensive, but the weight loss achieved is generally more permanent. However, as discussed in more detail later, some surgical treatments carry long term side effects, which may outweigh the benefits gained by the weight reduction. The question how to select patients for different types of treatment programmes is still largely unsolved and therefore it is important to try to identify biochemical or psychological factors, which may help to predict weight loss in the individual patient. Among the recognized predictive factors for the results obtained after conservative treatment are the basal metabolic rate, thyroid hormone status, initial body weight and adipose tissue cellularity (74, 75, 76), but the roles of other metabolic or of psychological factors in determining outcome of surgical treatments have not yet been established. Thus, apart from failures caused by surgical complications per se, it remains unclear why some patients do well and others poorly. Consequently, at present it is impossible to identify "unsuccessful" patients before surgery.

1.5.1 Conservative treatment

The ideal therapeutic approach to obesity would of course be to prevent it, and when obesity is manifest to try to stop it before it becomes morbid. If weight loss is achieved a new problem appears; to maintain the result. For these purposes an abundance of diets are available (77) and also pharmacologic therapies have been tried (78). However, morbidly obese subjects often have an addictive behaviour pattern, which is not as prominent among moderately obese individuals (13). The behaviour modification programmes (13) instituted to change problematic eating habits have been less successful in grossly obese patients on a long term basis and the majority of morbidly obese individuals need more drastic therapeutic interventions in order to loose weight. In these cases, only severe caloric restriction seems effective, but the results are generally transient. As mentioned earlier obesity is associated with a number of diseases, such a hypertension, diabetes, cardio-pulmonary disorders and an increased mortality. Treatment with diuretics and antidiabetic drugs is common in these individuals, who should in fact be treated not for complications to their obese state, but for obesity as such.

1.5.2 Surgical treatment

The first surgical approach to obesity was the intestinal bypass. Observations that patients lost weight after massive intestinal resections (in cases of mesenteric thrombosis, tumours, Crohn's disease etc) influenced Viktor Henriksson to perform small bowel resection to treat obesity in one case, which was cited by Hallberg in 1952 (79). The idea behind this method was to create severe malabsorption allowing the patients to eat freely. However, later studies (80) have demonstrated that the malabsorption following intestinal surgery is in most cases only transient; after some years practically all nutrients are absorb-

ed by the hypertrophic functional small bowel segment. Thus, most of the long term effects on weight reduction after this operative procedure seem to be consequences of a decreased food intake, probably due to the discomfort (diarrhoea and flatus), which is more prominent especially after a large food intake. Payne (81) in 1956 began a series of jejuno-colic bypass operations; he achieved a dramatic weight loss, but also increased postoperative side-effects, which made Sherman (82) propose jejuno-ileostomy as a more physiological shunting technique. Later on Payne suggested the end-to-side jejuno-ileostomy, which however in some cases led to inadequate weight loss. In 1971 Scott (83) reported on another modification with an end-to-end jejuno-ileostomy with end-to-side anastomosis of the bypassed small intestine to the sigmoid colon. Some of the existing intestinal shunts are shown in figure 1. The major

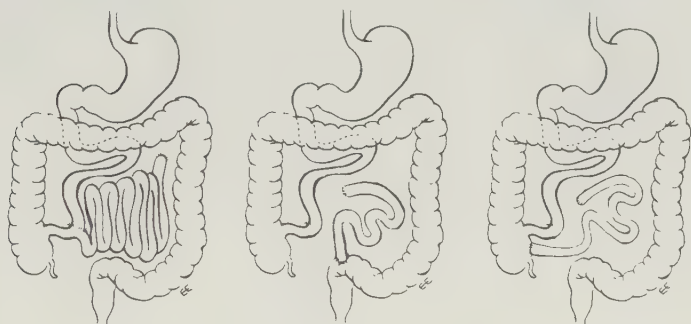


Fig 1. Some versions of intestinal shunts : end - to - side jejunoileostomy according to Payne (left) , end - to - end jejunoileostomy according to Scott (middle) and end - to - end jejunoileostomy according to Buchwald (right).

problem of all these alternatives were the side effects registered due to the blind loop (liver cirrhosis, electrolyte disturbances, high frequency of kidney and gall stones, diarrhoea etc), which made Eriksson (84) and Scopinaro (85) try two different principles for biliodigestive shunting of the blind loop (fig 2) in order to limit the bacterial overgrowth causing

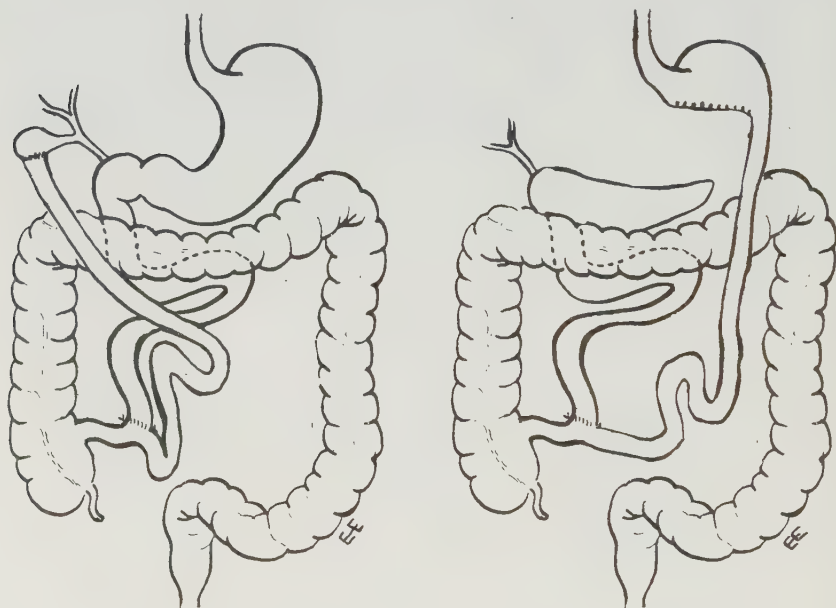


Fig 2. Versions of biliointestinal (Eriksson) and biliopancreatic (Scopinaro) shunts.

the undesired side effects. Excellent surveys in this field have been made by Hallberg (86) and Quaade (87). Approximately 100 000 patients have been subject to intestinal bypass surgery for obesity in the USA. The corresponding figure in Sweden is estimated at 2.000.

The increasing number of reports demonstrating undesired metabolic side effects after intestinal shunts made Mason and Ito start experimental studies in animals using gastric surgery to control obesity. These procedures aim at lowering food intake rather than to impair food absorption in the intestine. In 1969 Mason reported his first series on obese patients (88). Later, a great number of gastric procedures (89), including truncal vagotomy (90), have been tried in order to control the food intake among obese individuals.

The weight loss after gastric bypass procedures (fig 3) was

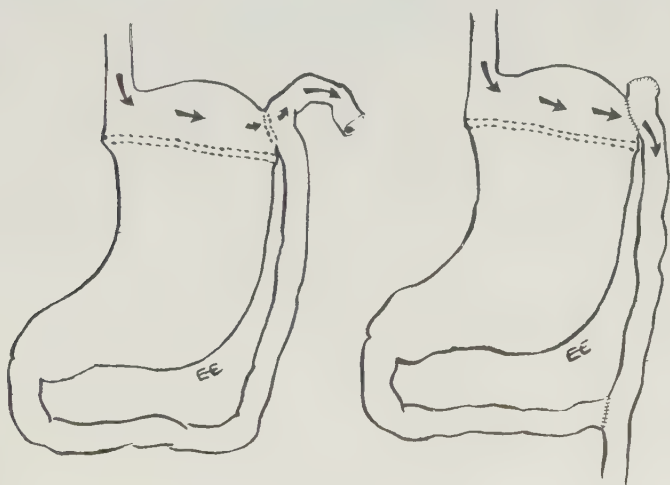


Fig 3. Two versions of gastric by pass.

reasonably good. However, the operative procedure was complicated to perform and the immediate postoperative complication rate was higher than after intestinal bypass. In 1976, Alden (91) introduced staple-machines in gastric bypass surgery, which made the surgical procedure safer and easier to perform. The gastric procedures did not lead to any of the serious metabolic complications seen as the result of the blind loop syndrome created in the jejuno-ileal bypass operations; i.e. patients lost after gastric by pass died in the early postoperative phase due to surgical technical complications, while fatal complications in patients operated on with jejunoileal bypass occurred months to years later due to metabolic disturbances.

In the beginning of the 70ies Gomez (92) introduced the gastroplasty procedure (fig 4), which kept the integrity of the upper

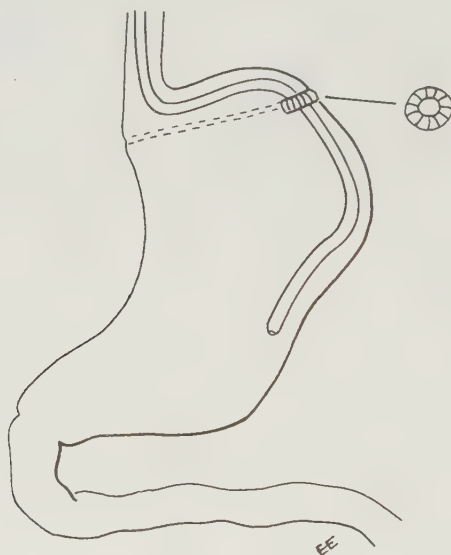


Fig 4 Completed gastroplasty

gastrointestinal tract; i.e. the food passes from the small gastric pouch of the upper part of the stomach through the small opening down the rest of the stomach into the duodenum instead of passing directly from the upper pouch to the small bowel as is the case in gastric bypass. The gastroplasty procedure allows postoperative endoscopic and contrast examinations of the antrum, pylorus and duodenum, which is nearly impossible after gastric bypass. The initial report by Gomez (92) showed few postoperative complications and a weight loss comparable to that after gastric bypass, but later studies have revealed great interindividual variability in weight reduction after gastroplasty, which is not as common after gastric bypass (93). Although severe metabolic disturbances, such as short bowel and blind loop syndrome complications, do not occur after gastric procedures for obesity, the surgical intervention may conceivably lead to profound alterations in nutritional pattern and upper gastrointestinal physiology. However, the short and long term metabolic and gastrointestinal effects of the gastroplasty procedure and the drastically reduced food intake after surgery have so far been poorly documented.

The more rarely used surgical treatments for morbid obesity, e.g. stereotactic operations in the central nervous system (94) will not be discussed in this paper.

2 AIMS OF THE PRESENT STUDY

- 1 To characterize the metabolic and psychological profile of massively obese persons before and after weight reduction by gastroplasty (I - V).
- 2 To evaluate the efficacy of gastroplasty on weight reduction and reduction in body fat/lean body mass (I).
- 3 To analyze the reasons for the wide variability in weight reduction after gastroplasty (I, V).
- 4 To identify early and late surgical complications to gastroplasty and other possible side effects, especially with regard to gastric function and morphology (I).
- 5 To describe the metabolic changes, especially in lipid and adipocyte metabolism, following weight reduction after gastroplasty; such data may help to differentiate between primary and secondary defects in obesity (II, III).
- 6 To identify the psychological sequelae which may follow great weight loss (IV).
- 7 To try to find metabolic, surgical or psychological factors predicting weight reduction after gastroplasty (V).

3.1 Patients

The patients included in the study came spontaneously to the surgical out-patient clinic or were referred there because of severe obesity. Age above 50, a history of myocardial infarction and diabetes demanding insulin treatment were considered contraindications for surgery. Patients with debility and known alcoholism were also excluded, as their cooperation in the post-operative phase might be insufficient. Prior to surgery the patients were subjected to a careful cardiopulmonary examination including ECG, spirometri, pulmonary X-ray and an evaluation by a trained anesthesiologist.

In total 24 patients (20 women and four men), between the ages of 23 and 44, took part in the study. Sixteen had been overweight since childhood and all had a history of intractable obesity and documentation of attempts at weight reduction with conservative treatment. Five patients developed their obesity during and after their first pregnancy. Two thirds of the patients suffered pain from weightbearing joints and many complained of social complications due their overweight. Three patients were treated with sulphonyl urea because of diabetes, and four had mild hypertension treated with β -blockers and/or diuretics. Except for the typical metabolic concomitants of obesity as such, none showed signs of severe metabolic or endocrine disturbances.

Before surgery, patients were encouraged to loose weight. Our lightest patient, a female nurse (height 157 cm), managed to reduce her weight from 110 to 93 kg and our heaviest patient reduced his weight from 220 to 192 kg. Mean weight reduction before surgery was 4 kg (range 0-28 kg). At operation the mean body weight was 128 kg (range 93-192 kg) and the mean Broca's index 2.1 (range 1.6-3.2).

3.2 Operative technique

All patients were operated upon 1979-1980 by the same operating team. A slight modification of the operative technique described by Gomez (92) was used. On the day before surgery the patient received water enemas in order to increase the surgical accessibility in the abdomen. To improve both the ventilatory exchange and exposition of the stomach the patient was placed in a reverse Trendelenburg position. An upper midline incision was used and the subcutaneous fat could nearly always be digitally pressed aside, thus reducing the subcutaneous bleeding. The preperitoneal fat was excised and in most cases a polytract-retractor set was applied. After incision of the triangular ligament of the liver and application of a rubber band around the oesophagus the fundus of the stomach was mobilized up to the oesophagus and all the vasa brevia were ligated. If the distance between the upper portion of the spleen and the stomach was short the use of hemoclips offered certain advantages. To avoid sliding of the clips, they were re-placed by ligatures after dividing the vessels. A small "window" was made at the lesser curvature close to the serosa of the gastric wall. By blunt dissection the posterior avascular space was entered and the TA-90 stapler was inserted from the lesser towards the greater curvature. In order to create the channel along the curvature the C-clamp attachment for the stapler was used, alternatively the five most distal staples were removed. The volume of the upper pouch was estimated by installing saline solution through a nasogastric tube. While performing the measurements the pouch was closed proximally by the rubber band around the oesophagus and distally by the TA-90 instrument. The volume was adjusted to 40-50 ml and the staple rows applied. Most of the patients received only one application of the TA-90 instrument (16 out of 21) because of an unexplicable leakage from the upper pouch in one of the first patients in our series, who received double applications of the stapling instrument. A large nasogastric tube (Charrieres 30) was inserted and a sero-

muscular suture, using 2-0 prolene, was applied around the tube forming an 11 mm channel. The large nasogastric tube was replaced by a smaller one to drain the proximal and distal parts of the stomach after the operation.

On rare occasions abdominal drainages were applied, but subcutaneous drainage as well as antibiotic prophylaxis with doxycycline and antithrombotic prophylaxis with dextran was routinely used. Ventilatory support was provided as indicated in the recovery room. Intensive care was not required. Postoperatively cimetidine was used during three days; thereafter the nasogastric tube was removed and the patient received a liquid diet followed by pureed diet after one week. In their normal environment the patients had to adjust to a drastically reduced food intake (700 - 1000 kcal/day) and they were given supplementation with vitamins B₁₂, folic acid and iron if any deficiency was detected.

3.3 Follow-up

On or before admission to hospital all aspects of the metabolic studies and surgical procedure, including mortality and morbidity, were discussed with the patients. On admission, the last 21 patients underwent extensive metabolic, gastrointestinal and psychological investigations. On dismissal from hospital, the patients were instructed to avoid whole meat, vegetables of threadlike structures and to take frequent small meals and to drink between meals. The routine postoperative follow up included a monthly visit to the out-patient clinic for the first three months and a visit every three months thereafter until 18 months after surgery. Complete postoperative clinical, metabolic and gastro-oesophageal investigations were performed preoperatively and 6-8 months after surgery in 21 of the patients and repeated 12-18 months thereafter in 13 patients, as two patients became pregnant and another six refused to repeat the last follow up

examination. The first two patients in our series of 24 were only followed with regard to weight reduction and one patient died from pulmonary embolism in the early postoperative phase.

3.4 Gastric morphology and function

Endoscopic examinations (P2 gastroscope, Olympus, diameter 7 mm) were carried out pre- and postoperatively by a surgeon from the operating team and included biopsies from the distal oesophagus, cardia and antrum. Upper G-I series were performed according to routine procedures. Channel dilation was considered to have occurred if the channel width was twice that of the gastroscope diameter. In these patients, the contrast medium disappeared immediately from the upper pouch during the upper G-I series. Dilation of the pouch was estimated by evaluation of the gastroscopy and X-ray examinations. Oesophageal manometry including reflux provocation was carried out according to Sandmark (95). Basal and stimulated gastric acid secretion were studied using a pentagastrin load (6 µg/kg body weight) for the stimulation test. At the follow-up examinations the nasogastric tube for the sampling was inserted into the lower part of the stomach with the aid of a leader using x-ray guidance.

3.5 Metabolic investigations

Body compartments and fat cell size.

Body fat and lean body mass were calculated from determinations of endogenous ^{40}K . Lean body mass was then estimated by the formula described by Forbes (96, 97). Body fat was calculated by subtracting lean body mass from the body weight. Fat cell size was determined in surgical biopsy specimens obtained from gluteal

fat. Adipocytes were isolated from the biopsy material by collagenase treatment (98). Fat cell size was measured on 100 cells from each sample under the light microscope. From the mean cellular diameter mean cell volume and triglyceride content were calculated.

Plasma lipids, lipoproteins and lipolytic enzymes

HDL cholesterol was determined in the clear supernatant obtained after precipitation of VLDL and LDL by $MgCl_2$ and dextran sulphate (99). Triglyceride and cholesterol were determined by enzymatic methods (100, 101). LDL cholesterol was calculated according to the formula of Friedewald et al (102) modified to SI units. LPL activity in adipose tissue was determined in surgical biopsies of gluteal fat after elution with heparin (103, 104). LPL activity in adipose tissue was related to tissue weight and also expressed per cell. LPL and hepatic lipase (HL) activities were determined in postheparin plasma drawn 15 minutes after the injection of 50 U heparin/kg body weight (105).

Glucose and lipid load

Glucose tolerance was estimated from an intravenous glucose load. Intravenous administration was preferred to oral intake as many of the patients postoperatively may have had difficulties to swallow the necessary amount of glucose solution during the stipulated time. Blood glucose was measured by the glucose-oxidase method. Plasma insulin (106) and glucagon (107) were determined by radioimmunoassay. The intravenous fat tolerance test (IVFIT) was performed as described by Carlsson & Rössner (108).

Microcalorimetry

Microcalorimetry was performed as described by Monti et al (109) on gluteal adipocytes taken by open surgical biopsies in local anesthesia. Two microcalorimeters of the thermopile heat conduction type were used (20, 110). In order to improve the accuracy of the measurements the number of cells were determined in each individual sample (for details see III). The heat production values obtained were related to variables reflecting glucose metabolism and thyroid function, which may be of importance for the metabolic activity and cellular heat production.

Various methods

Variables reflecting thyroid function were determined according to the methods described in the individual papers. Hematologic data including S-cobalamines and B-folate, S-kreatinin, S-iron, S-TIBC, S-ferritin, S-gastrin, electrolytes, minerals, uric acid and variables reflecting liver function were determined according to routine techniques in our laboratory.

β -endorphine like material was analyzed by a specific β -endorphine radioimmunoassay (111).

3.6 Psychological testing

The psychological investigation particularly stressed the patients' defensive organization, i.e. their behaviour when exposed to environmental pressure and stress. Also their self perception and cognitive characteristics, which reveal the level of maturity and dependence upon influences from persons in their environment, were tested. The postoperative testing

programme also aimed at identifying social and psychological concomitants to weight reduction. It included an interview, a clinical rating and further psychological evaluation using the Rod-and-Frame test (RFT)(112, 113) and the Meta-Contrast-Technique (MCT) (114, 115, 116, 117). The results were compared to test results obtained before surgery and correlated to alterations in different metabolic variables following weight reduction (for details see paper IV and V).

3.7 Statistical evaluation

The experimental data have been compared to the reference ranges routinely used at the laboratory or, when indicated, to a control group of twelve normal weight individuals matched for age and sex. The main emphasis, however, has been put on the evaluation of differences between preoperative values and values obtained at follow up, which were analyzed using Wilcoxon's rank order test for paired observations. This longitudinal design, in which interindividual variations are eliminated, makes it easier to specify effects of obesity on various parameters. Correlations between variables, including the relationships between the changes in such variables, were calculated using Spearman's rank correlation test. Again, the longitudinal design allows more strict evaluation of the relation between metabolic and morphometric data in our obese patients.

Two-way analysis of variance (118) was used for evaluation of the differential weight loss in paper IV and V, where differences between groups for psychological variables were evaluated using Fisher's exact test of 2×2 tables.

Studies in humans are often limited by the number of patients available. However, when a large number of subjects is required to yield significant differences, the clinical value may be less

important. Significant results obtained with a small sample may be accidental and to be regarded as safe they must be coherent and interpretable.

4 RESULTS

4.1 Metabolic and psychological observations prior to surgery.

Before surgery all patients were severely obese; body weight was 93 - 192 kg (mean 128 kg) and Broca's index 1,6 - 3,2 (mean 2,1). Body fat varied between 47 and 128 kg (mean 72 kg) and mean lean body mass (LBM) was 56 kg (range 45 - 68 kg). The gluteal fat cell size was above the reference range in all subjects except one. A comparison of body fat, body weight and fat cell size indicates that all patients represented a mixed type of obesity, i.e. they had an increased number of enlarged fat cells.

Preoperatively, variables reflecting liver function were frequently above reference range and almost 1/3 of the patients had one or more variables outside the reference ranges.

Disturbances in lipid transport were indicated by hypertriglyceridemia in five patients and a mean P-cholesterol in the upper reference range. Two subjects had elevated levels of LDL cholesterol and two had HDL cholesterol concentrations below the reference range leading to an elevated LDL/HDL ratio. Lipoprotein lipase activities, measured in postheparin plasma, tended to be low. Adipose tissue LPL activities, whether measured per g tissue or per 10^6 cells, were within the normal range.

Variables reflecting carbohydrate metabolism indicated decreased peripheral insulin sensitivity. The mean fasting blood glucose levels were above the reference range and five individuals showed

in fact values above 6,0 mmol/liter. Six subjects had hyperinsulinemia, whereas three patients has increased fasting glucagon levels prior to surgery. The individual measurements reflecting glucose metabolism, especially P-insulin, showed an extreme interindividual variation.

Hematologic variables (including S-iron, S-cobalamines, S-ferri-tin and B-folate), electrolytes, minerals, uric acid, S-creatinine and variables reflecting thyroid function were within the normal range before surgery.

In the psychological tests this obese group was characterized by signs of immature sense of self and of anxiety, and by using regressive defences, i. e. coping strategies which are normally abandoned during childhood. No gross deviations from average performance were found in tests estimating general intellectual capacity (for details see IV and V).

4.2 Weight reduction

As mentioned earlier, patients were encouraged to reduce weight preoperatively; mean weight loss before surgery was 4,0 kg and total mean weight loss 18 months after surgery 34,4 kg. However, there was a marked variation in weight loss after surgery. The average weight reduction (preoperative weight loss excluded) is shown in Figure 5 as well as change in lean body mass and body

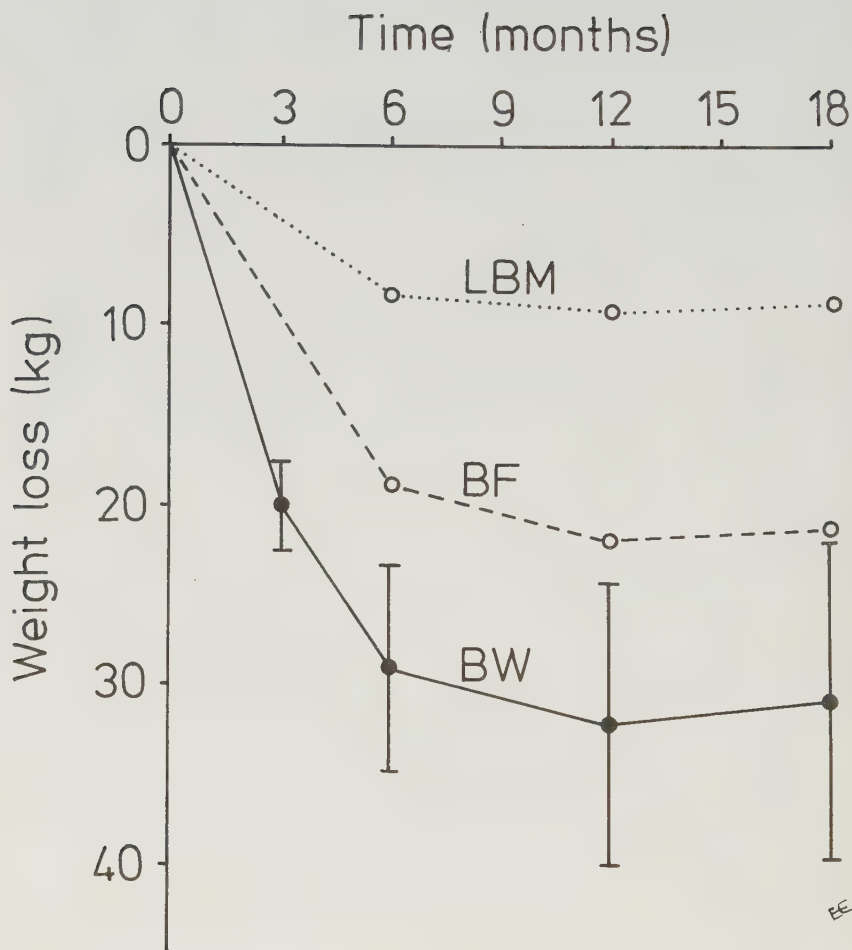


Fig 5 Reduction in body weight (BW), lean body mass (LBM) and body fat (BF) (mean $\pm$ SD) in 23 obese subjects after gastroplasty operation (preoperative weight reduction not included). At operation the initial weight was 128 ± 21 kg. The mean weight reduction before surgery was 4 kg (0 - 28 kg).

fat. The initial weight loss was rapid and six months after the operation the mean weight loss, preoperative weight loss included, was 33 kg (range 12 - 53 kg); about 70 % could be accounted for by a loss in body fat. Eighteen months postoperatively we found a total mean weight loss of 34,4 kg (range 1 - 72 kg). After an initial substantial weight loss three patients started regaining weight six months after surgery and 18 months postoperatively they had almost reached their initial body weight. In total 30 % of the patients had unsatisfactory weight reduction (less than 20 % weight reduction after 18 months).

4.3 Clinical observations

The patients reported a feeling of satiety after their small meals and they did not feel severe hunger in spite of low daily caloric intake. During the first months after surgery, until they had learned to adjust their food intake, all patients had a tendency to vomit. In two patients, frequent prolonged vomiting led to swelling of the channel causing temporary gastric retention. They required short readmission to the hospital for intravenous fluids due to hypocalcemic metabolic alkalosis. Endoscopic or surgical intervention was never required. Loss of hair, occasional headache, and constipation were complaints from about 1/3 of the female patients. Some patients had large difficulties to adopt new eating habits. For example, one patient consumed large quantities of mayonnaise directly from tubes, when the altered conditions in his stomach did not allow him to eat solid food without vomiting. Two patients became pregnant 9 - 12 months following surgery. The pregnancies were well tolerated and free of complications.

4.4 Early surgical complications

One patient died in a massive pulmonary embolus about 20 hours after surgery; in this case a cholecystectomy was also performed. Two patients had to be reoperated on, drained and supplied with a temporary Witzel fistula because of a leakage from the upper pouch two and three days after surgery. After reoperation they both had uneventful but protracted postoperative courses. Two accidental splenectomies were performed. One patient developed a deep iliac vein trombosis, which was surgically removed.

4.5 Late surgical complications

The frequency of verified staple line ruptures/dilation of the channel or dilation of the upper pouch, as demonstrated by gastroscopy and/or upper G-I series, is shown in Table I. The

Table I

Distribution of late postoperative complications in patients with differential development of weight loss 18 months after surgery.

	Body weight loss in % compared to bod weight at surgery		
	> 40	20 - 40	< 20
Number of patients	4	12	7
Enlarged channel	2	3	7
Enlarged pouch	2	1	-

channel dilations were due to staple line rupture or the fact that the prolene suture slipped through the wall, which ruins the stability of the channel. This complication was discovered at the second check up about 12 months after surgery and the patients could often tell at what time they had been able to eat without restrictions. Channel dilation occurred in three of the five patients, who received two applications of the TA 90 instrument and in nine of the 18 patients receiving only a single staple application. The weight reduction and the frequency of late surgical complications were similar in patients operated early and late in the series. It should be pointed out that also some patients with verified staple line rupture/channel dilation lost weight successfully; five patients with dilation of the channel had a weight reduction exceeding 20 % 18 months after surgery.

4.6 Gastric morphology and function

Eighty per cent of the patients had an elevated stimulated gastric acid secretion preoperatively. Thirty per cent also had an increased basal acid secretion. At endoscopy 1/3 of the patients had minor gastritis, which was confirmed by histology from the gastric mucosa. Postoperatively the high acid secretion decreased in all patients except two. At endoscopy after surgery there were no visual or histological signs of more severe gastritis than before the operation. The serum levels of gastrin remained within the normal range. Oesophageal manometry including reflux provocation was normal and did not change after surgery.

4.7 Psychological considerations and sequelae

In the preoperative tests, the obese patients frequently showed signs of immaturity and anxiety, which decreased in the postoperative tests. After weight reduction signs of depression occurred; 2/3 of the patients were scored for depression in psychological tests as compared to none before surgery. Four patients showed severe depression including suicidal thoughts. The depressive trends were most prevalent in the patients, who lost most weight.

Trends, however not significant, were found implicating that the patients who developed depression more often had a childhood onset of obesity. No correlation was found between surgical complications or metabolic disturbances after gastroplasty and postoperative depression, implying that these factors do not influence the patient's postoperative psychological status. Patients, who lost weight successfully, had more mature psychological defences, were significantly older and accepted a personal responsibility for the outcome of treatment. They were generally satisfied with the outcome of surgery. Patients, who failed to loose weight satisfactorily had less mature defences, that is they could not cope with environmental stress as normal grown up individuals, were less able to tolerate food restriction and tended to regard the negative outcome as outside their own control.

4.8 Biochemical alterations

The different biochemical and morphometric variables analyzed before and at follow up 6 - 8 months after surgery are shown in Table II.

Variable	Reference range	I	II	I vs. II
B-hemoglobin	115-163	142.4±13.4	135.6±15.9	p<0.05
B-erythrocyte count, no./l	3.7-5.4×10 ¹²	4.75±0.37	4.61±0.41	p<0.05
B-erythrocyte volume fraction, %	37-49	41.6±3.8	39.9±4.6	p<0.05
S-iron, µmol/l	10-30	23.4±7.6	18.9±8.7	p<0.05
S-ferritin, µg/l	>10	48±55	31±33	p<0.05
S-cobalamines, pmol/l	110-650	372±105	282±125	p<0.005
B-folate, nmol/l	70-200	138±45	75±29	p<0.005
P-triglyceride, mmol/l	0.3-2.1	1.9±1.2	1.3±0.8	p<0.005
P-cholesterol, mmol/l	3.2-7.2	5.6±1.1	5.0±1.0	p<0.01
P-HDL cholesterol, mmol/l	0.8-1.7	0.96±0.20	1.03±0.31	n.s.
P-LDL cholesterol, mmol/l	1.3-4.5	3.66±1.06	3.10±1.15	p<0.025
LDL/HDL ratio	<3.5	3.9±1.5	3.2±1.8	p<0.025
B-glucose, mmol/l	3.3-5.6	6.3±2.3	4.5±0.6	p<0.005
P-insulin, µU/ml	5-25	21.6±17.2	9.5±6.5	p<0.025
P-glucagon, µg/ml	50-250	193±94	119±89	p<0.025
S-bilirubin (total), µmol/l	3-20	13.6±3.6	10.6±4.6	p<0.01
S-alkaline phosphatase activity, µkat/l	0.8-4.6	3.37±0.75	2.7±0.56	p<0.005
S-γ-glutamyl transferase activity, µkat/l	<1.0	0.52±0.56	0.29±0.16	p<0.025
S-asparagine aminotransferase activity, µkat/l	<0.67	0.67±0.66	0.39±0.18	p<0.025
S-alanine aminotransferase activity, µkat/l	<0.67	0.73±0.79	0.27±0.23	p<0.005
S-T3 (nmol/l)	1.5-3.0	2.2±0.4	2.2±0.4	n.s.
S-T4 (nmol/l)	51-154	128±20	117±18	p<0.05
S-rT3 (nmol/l)	0.14-0.54	0.26±0.6	0.23±0.6	p<0.05
S-TBPM (arb U)	0.8-1.2	0.95±0.13	0.88±0.13	p<0.05
S-TSH (U/l)	0-8	3.13±1.36	3.0±0.85	n.s.
S-TBPA (µg/ml)	180-300	242±38	202±57	p<0.005
S-TBG (µg/ml)	12-24	20.55±4.2	20.56±3.0	n.s.
S-FT ₄ (nmol/l)	16-30	30.7±3.9	29.6±5.3	n.s.
Postheparin plasma LPL activity (mU/ml)	70-145	61.9±19.4	52.9±16.1	n.s.
Postheparin plasma HL activity (mU/ml)	320-620	498±205	364±246	p<0.005
IVFTT: k ₂ value (% per min)	2.2-7.4	4.77±1.62	6.12±1.85	p<0.005
Adipose tissue LPL activity (mU/g tissue)	5.2-14.8	6.6±1.6 ¹		
Adipose tissue LPL activity (mU/10 ⁶ cells)	2.1-5.9	4.2±1.0 ¹		

¹ mean ± SEM.

Table II Biochemical variables before gastropasty (I) and at follow up 6 - 8 months postoperatively (II). Data are given as mean ± SD.

4.8.1 Haematology

B-hemoglobin decreased by about 5 % at follow up, but none of our patients developed an anemia during the follow-up period. S-iron concentrations decreased significantly in parallel with S-ferri-tin levels. In three patients S-iron levels were reduced below the lower reference limit. Also S-cobolamine and S-folate levels decreased markedly and six patients had B-folate concentrations below the lower reference limit six months following surgery.

4.8.2 Liver function

Variables reflecting liver function improved considerably at follow-up and seven patients, who preoperatively had one or more variables outside the reference range, normalized postopartively.

4.8.3 Thyroid function.

S-T4 and S-rT3 decreased marginally but significantly at follow-up in the subgroup of patients participating in the microcalori-metric measurements (III). The same trends were also found in the group as a whole (I), whereas S-T3 levels remained unchanged after surgery.

4.8.4 Lipid metabolism.

Four out of five patients with hypertriglyceridemia before surgery normalized after surgery. In fact P-triglyceride levels decreased postoperatively in all patients. The mean reduction in P-triglyceride concentration was about 30 %, which remained also at follow-up 18 months after surgery. A 12 % significant decrease

in plasma cholesterol levels was registered and maintained at least 18 months after surgery. The fall in plasma cholesterol levels could be entirely accounted for by a decrease in plasma LDL levels. The moderate rise in HDL cholesterol levels did not reach statistical significance but was maintained at the 18 months follow-up. The LDL/HDL ratio decreased by 18 % 6 months after surgery. These changes were significantly correlated to the reduction in body weight/body fat (for details see II).

The mean activity of LPL in postheparin plasma decreased post-operatively although the decrease did not reach statistical significance. The hepatic lipase (HL) activity in postheparin plasma decreased after weight reduction by 7 %, which was highly significant. An increase of the elimination rate of exogenous triglyceride (IVFII) was found after weight reduction.

4.8.5 Glucose metabolism.

The mean fasting blood glucose levels were increased before surgery and decreased significantly at follow-up. Five individuals with elevated fasting blood glucose levels all improved at follow-up. There was a significant reduction in insulin levels after treatment and five of the six individuals with overt hyperinsulinemia before treatment normalized following surgery. Similarly, mean plasma glucagon concentrations were in the upper part of the normal range before treatment and decreased significantly after surgery. Three of our patients had increased fasting glucagon concentrations before weight reduction; one was normalized after treatment. Blood glucose pattern as well as plasma insulin and plasma glucagon pattern improved significantly as registered during the glucose load (Fig 6). The

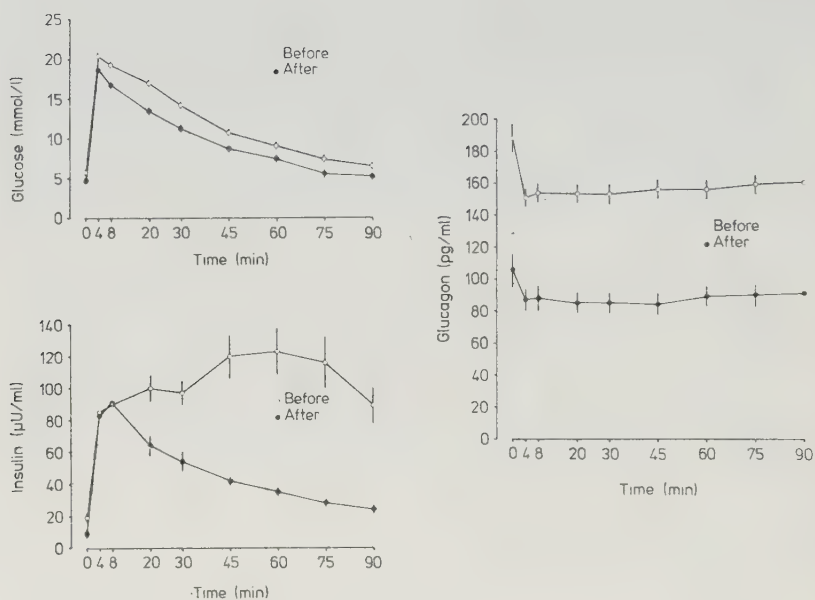


Fig 6. Blood glucose, serum insulin and plasma glucagon levels in 15 patients during an intravenous glucose load before gastropasty and at follow up 6-8 months postoperatively. Data are given as mean $\pm$ SEM.

decrease in plasma levels of insulin was significantly correlated not only to the reduction in body weight/body fat, blood glucose and plasma glucagon but also to the decrease in plasma cholesterol and plasma triglyceride levels and also to the increase in plasma HDL levels (for details see paper II).

4.8.6 Adipocyte heat production

About 70 % of the weight loss among the patients could be accounted for by a reduction in body fat. Fat cell size decreased by 13 %, which was highly significant. The heat production in adipocytes, whether expressed per cell or per gram fat tissue, was significantly lower in our obese subjects than in lean individuals before surgery. After weight reduction, heat production in adipocytes increased considerably and normalized (Fig 7).

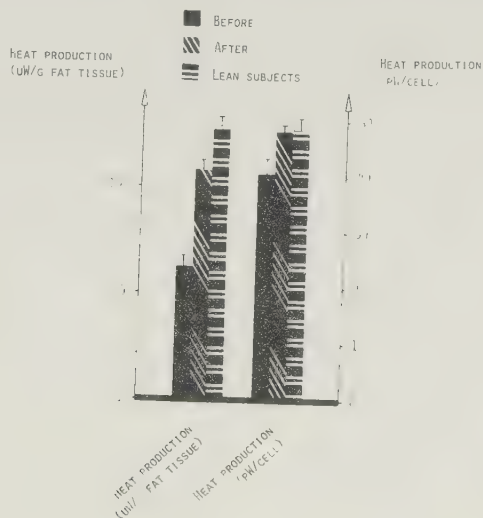


Figure 2 Adipocyte heat production in lean subjects and in obese patients before and after weight reduction by gastroplasty. Data are given as mean $\pm$ SEM.

An analysis of the relations between heat production values and morphometric data demonstrated that the increase in heat production was correlated to the decrease in body weight and also to certain variables reflecting thyroid function (for details see III).

4.8.7 Various laboratory tests.

Except for transient hypokalemia in two patients suffering from prolonged vomiting two to three months after surgery serum levels of sodium, potassium and calcium were essentially unchanged. There was a significant reduction in S-magnesium levels, although none of the patients developed hypomagnesemia. One of the vomiting patients developed a transient hyperuricemia, but at follow up there were no signs of hyperuricemia for the group as a whole.

S-creatinine decreased significantly at follow-up, probably due to the reduction in lean body mass, reflecting a loss of muscle tissue.

4.9 Prediction of weight loss.

As stated earlier there was a wide range in weight reduction after surgery. Although the patients with the least weight reduction had all developed channel dilation, several patients with great weight loss 18 months after surgery also showed dilation of the channel, indicating that the wide range in weight reduction could not unequivocally be attributed to technical - surgical factors. A number of morphological and biochemical variables including initial body weight, fat cell size, and variables reflecting thyroid function, lipid and glucose metabolism and adipose tissue metabolism were not related to subsequent weight

loss, i.e. they had no predictive value for the weight loss obtained. However, an extensive psychological investigation performed before surgery demonstrated significantly more signs of sensitivity and denial in the unsuccessful patients, who also were younger, more immature and had a higher estimated alcohol consumption. The successful patients were significantly older, had more mature psychological defences and tended to live in, and to be dependent upon, a supportive social environment.

5 DISCUSSION

5.1 Methodology and experimental design.

The present investigation was carried out between January 1979 and July 1982; i.e. the last patient in this serie was operated in November 1980. In the end of the 70ies the serious metabolic complications seen as the result of the blind loop syndrom created in the jejunoileal bypass operation, were well known(87, 119). The gastric bypass operation, which was developed and introduced at this time, eliminated these complications, but the immediate postoperative complication rate after this procedure was higher than after intestinal bypass. The weight reduction achieved with the two techniques was comparable (120, 121). The next step in the development of gastric surgery to control morbid obesity, the gastroplasty, had the advantage of keeping the integrity of the upper gastrointestinal tract and allowed postoperative gastroscopic and X-ray examinations of the lower part of the stomach and duodenum, which was nearly impossible after gastric bypass. The earliest reports with this new method also showed few postoperative complications and a weight loss comparable to that after gastric bypass (92, 122). These attractive preliminary results made us initiate a more detailed evaluation of the horizontal gastroplasty introduced by Gomez (122).

The studies have been focused on the clinical results of treatment, on the metabolic effects of weight reduction after gastroplasty, and on the psychological sequelae to treatment. Earlier evaluations of treatment programs obesity have generally been designed to cover only one of these aspects. The broad approach used in the present study would allow a simultaneous registration, in the same patients, of clinical, biochemical and psychological variables, so that possible relationships between these different aspects could be analyzed.

In the initial reports on weight reduction after gastroplasty, channel and pouch dilations were found responsible for the failure to loose weight among the patients. However, the number of patients lost to follow-up was often considerable (122) and only patients with inadequate weight loss were subjected to X-ray and/or endoscopic examinations. Consequently, in earlier reports, the number of channel (and pouch) dilations following surgery may have been underestimated. To avoid this source of error we decided to control all patients at regular intervals postoperatively.

In most reports on weight loss following gastric or intestinal surgery for morbid obesity, weight reduction is simply given as kg body weight lost following the surgical procedure. In the present study we were able to differentiate between weight reduction due to a loss in body fat (which is the aim of treatment) and lean body mass. The lack of data in this study regarding the distribution of the adipose tissue is explained by the fact that the full relevance of this information was not known, when this study was performed (33, 123).

One of the purposes of this investigation was to compare the metabolic profiles of our obese patients before and after weight reduction. These measurements were selected for three purposes: first, to study possible negative metabolic effects of treatment,

such as the development of deficiencies of nutrients or vitamins or derangement of electrolyte balance; second, to register expected improvements of the metabolic changes accompanying obesity, with special emphasis on cardiovascular risk factors such as aberrations in glucose and lipid metabolism; and third, to evaluate parameters which have been suggested to play a primary role in the development of obesity (LPL activity, cellular thermogenesis). The data have been collected to allow comparison with results obtained by other methods for weight reduction (124). The fact that the patients were encouraged to loose weight to facilitate surgery led to a mean weight reduction of 4 kg, which may have influenced preoperative data, i.e. make the differences in metabolic observations obtained less conspicuous. In order to eliminate other effects due to changes in caloric intake, the patients were hospitalized one week during the performance of the measurements and given a standard dietary regimen. It was not possible to standardize in relation to menstrual cycle. Eight of our patients did not participate in the metabolic follow-up 18 months after surgery: two became pregnant, one lived far away and the others refused to repeat the extensive follow-up program.

The oesophageal manometry was carried out according to Sandmark (95), in order to identify patients with asymptomatic reflux as there had been reports on postoperative heart burn and regurgitation in patients treated with gastroplasty (125).

The direct microcalorimetry used in the present investigation to measure heat production from adipocytes has been developed in our group (109) and has earlier proven a reliable analytic tool with satisfactory precision and reproducibility for comparison of the total metabolic activity in different cell populations during steady state conditions (58). The sensitivity of the instrument allows registration of heat production corresponding to temperature differences of 10^{-7}°C , i.e. the heat output of 50 000 cells (around 3 mg lipid) can be monitored with great accuracy. It is

therefore a promising tool for the study of the regulation of cellular energy metabolism. Combined with measurements of concentrations of substrates and appropriate metabolites, the technique can also be used for the evaluation of metabolic efficiency.

The psychological methods (MCT and RFT) used to obtain objective data before and after surgery have earlier demonstrated their diagnostic efficiency in clinical studies (112, 115, 117). They were chosen to evaluate the patients behaviour when exposed to stress (MCT) and also their dependence upon influences from persons in their environment (RFT). In addition to these objective tests a careful clinical interview was undertaken covering the patients childhood conditions, relations to parents and their more or less successful development towards social and emotional independence. In many reports questionnaire data and clinical interviews have been the only tool to evaluate and compare the psychological profile of the patients before and after treatment for morbid obesity. We believe that some patients, pleased with the many positive effects related to their weight reduction, tend to deny or deemphasize the negative psychological effects experienced after treatment, when subjected to non objective follow up examinations (questionnaire, clinical interviews).

5.2 Results.

In a longitudinal experimental design, as used in the present investigation, each subject represents his own control and the influence of inter-individual biological variation is largely eliminated. The effects produced by an intervention (in this case a surgical procedure) can be quantitated and relationships between variables (e.g. metabolite concentrations and body weight) are easier to identify than in a cross-sectional approach. The

number of individuals required in longitudinal studies is generally smaller and the use of paired statistical tests gives a satisfactory sensitivity and precision in the analysis of data.

5.2.1 Early surgical complications

Surgery on morbidly obese patients is risky even if careful preoperative selection is undertaken. The incidence of pulmonary embolus and deep vein thrombosis is increased and among our patients two such complications, one of which was mortal occurred in spite of thrombotic prophylaxis with dextran. Also infection rate and respiratory problems (which could be avoided among our patients) may follow surgery on these individuals, even if they, as was the case with our patients, are treated with prophylactic doxycycline.

Although gastroplasty is easier to perform than gastric bypass it is not without surgical complications. Two patients early in our series of operations suffered splenectomy due to accidental tear on the splenic capsula, which did not stop to bleed. Perforations of the upper pouch are serious and well known from the literature (93, 122). These leakages are mostly unpredictable. Inadequate double application of the staple rows, extensive devascularisation of the major curvature leading to ischemia of the upper pouch or an improperly located nasogastric tube might be the causes of these perforations. Early detection using clinical parameters (especially fever and tachycardia) and immediate reoperation and drainage, including the use of a Witzel fistula, contributed to an uneventful but protracted postoperative course in our two patients with this serious complication.

5.2.2 Weight reduction and late surgical complications

With all types of conservative or surgical therapy programmes there are wide interindividual variations in the result of treatment with respect to weight loss. Long term conservative treatment (fasting, diets) and also jaw wiring (126, 127, 128), lead to considerable weight reduction, which, in nearly all cases, is impossible to maintain. Patients subjected to intestinal bypass surgery often restrict their food intake due to the increased discomfort (frequent diarrhoeas and flatus) experienced after large meals (80). In general, weight reduction after intestinal bypass was adequate, but the frequent and serious metabolic side effects (87) made it unsuitable for many patients. The gastric bypass procedures also lead to an adequate weight loss. Following gastric procedures to control obesity, food intake is strictly limited as long as the conditions created at surgery in the upper gastrointestinal tract remain intact and the patients must adapt new eating habits. Among our 23 patients seven showed unsatisfactory weight reduction (less than 20 % weight loss 18 months following surgery), which was discouraging, but consonant with other recent reports (129, 130). Other authors report better results (92, 122), but have an unacceptably large proportion of patients who did not participate in the follow-up.

The mean body weight reduction among our patients at the six months follow-up was 24 % compared to body weight at surgery. Eighteen months after surgery mean body weight reduction was 27%; i.e. most of the weight reduction occurred during the first six months following surgery, but the range in weight reduction 18 months postoperatively was 1 - 71 kg. In this study, as after weight reduction by fasting (124, 131), 70 % of the weight loss could be accounted for by a loss in body fat. Most of the wide variations in weight loss could be explained by dilation of the channel leading from the upper pouch to the lower part of the stomach; this complication was usually discovered 6 - 12 months

after surgery. All seven patients with a weight loss below 20 % 18 months postoperatively had channel dilation. However, five patients showed a weight loss exceeding 20 % in spite of channel dilation. Apparently they were able to adhere to a more strict diet, perhaps because of the satisfaction felt after the initial weight loss. This finding suggests that psychological factors may be important for successful weight loss after gastroplasty (see below). We found no correlation between the incidence of channel dilation and technical difficulties at surgery. There was no accumulation of patients with staple line rupture/channel dilation early in the operation series, which could have been an explanation to the high incidence of this complication, as we had little experience from bariatric surgery prior to this investigation. Thus, it is possible that channel dilation occurs among certain patients, who are unable to comply with the restrictive postoperative regimen; i.e. the staple rupture and the following channel dilation may occur due to excessive uncontrolled food intake. This interpretation is consonant with the finding that about 40 % of patients admitted for revision of their gastroplasty remain unsuccessful with regard to weight reduction even after a second operation (122). We also believe that other reports may underestimate the frequency of this late postoperative complication unless all patients, also those who loose weight successfully, are followed with postoperative gastroscopy or an adequate upper G-I series.

5.2.3 Psychological sequelae.

Most of the obese patients referred for surgical treatment have a history of repeated failures to comply with diets, i.e. to tolerate the experience of food restriction. The patients desire for gastric surgery may seem illogical in these cases, as psychological crises might be expected when these patients, due to the gastric procedure, are forced to adopt radically new eating

habits. However, in the preoperative opinion of these patients, weight reduction would strongly improve their psychological status. Some investigators (71, 73) report postoperative psychological crises (involving depression, anxiety and marital problems) in many patients after weight reduction achieved by surgery, while others emphasize the psychosocial benefits experienced by the patients after successful weight reduction (6, 5, 66, 68).

The psychological test protocols of our patients differed from normal weight individuals by showing more signs of immaturity, i.e. they often demonstrated coping strategies, which are normally abandoned during childhood.

The psychological sequelae in subgroups of patients showing a more or less successful weight reduction differed significantly. 2/3 of our patients were scored for depression and 1/5 developed acute depressive reactions, and the depressive reactions were more prevalent in the patients who lost most weight. This could at least theoretically be attributed to early or late surgical complications or to the more pronounced metabolic disturbances following marked weight reduction. However, no such correlations could be found. The high frequency of postoperative depressive reactions in our material is inconsistent with many reports based on questionnaire data, but is consonant with evidence obtained in studies where the postoperative adaptation has been followed more closely (62, 132). The fact that patients with psychological problems tend to be underrepresented in follow-ups (59) (refuse to answer questionnaires) and that many patients, pleased with the many positive effects related to their weight loss, tend to deemphasize or deny any negative effects may explain the conflicting data. Self ratings may in such cases produce misleading data. On a common sense basis, it may be expected that the patients, who did not lose weight satisfactorily would experience more severe psychological problems. The opposite outcome found here and in other studies (62, 132) indicates that

a rapid and substantial weight loss and/or enforced reduction of food intake involve problems of adaptation.

5.2.4 Biochemical alterations

Data obtained in our patients before weight loss confirm the general metabolic pattern described in numerous reports (24, 124, 133). The combination of hyperinsulinemia, fasting hyperglucosemia and a decreased glucose tolerance is consistent with a decreased insulin sensitivity among obese individuals. The lipoprotein profile had a supposedly atherogenic pattern with an elevated LDL/HDL ratio.

In the present investigation most patients lost weight rapidly. Weight reduction and also the metabolic changes registered varied considerably, but it should be pointed out that almost all patients were overweight also at follow ups postoperatively. The biochemical alterations seen in obese individuals are generally assumed to be consequences of the obese state or of an augmented food intake. Consequently, the biochemical alterations after bariatric surgery may be related to changes in body compartments or consequences of the drastically reduced food intake. However, some authors (22) claim that disturbances in the LPL activity in adipose tissue remain in ex-obese patients and thus may play a primary role for the development of obesity.

The surgical procedure as such, as is the case with intestinal bypass, may also lead to undesired metabolic changes, as is the case with intestinal bypass procedures creating blind loop syndromes. Most of the biochemical consequences following weight loss seem to be favourable, regardless the method used to achieve weight reduction (124). In the gastroplasty procedure no blind loops are created, but the surgical intervention could at least theoretically lead to disturbances in gastric acid secretion or

alterations in gastric morphology. In this study no such negative changes were found. On the contrary, basal as well as stimulated gastric acid secretion decreased in most patients, probably due to the fact that their gastric volume was above average before gastroplasty with a corresponding increase in the amount of parietal cells. After surgery the stomach was not stimulated by a large food intake and consequently parietal cell mass was reduced.

Some of the side effects registered, such as moderate decreases in the levels of S-cobalamines, S-iron and B-folate, are most likely due to the drastically reduced food intake. No anemia or neuropathy was registered, probably because the patients were given supplementation when their deficiency was detected. However, it cannot be excluded that these patients, due to a reduced food intake, may in the long run suffer from iron, vitamin and trace element deficiencies as also indicated in this and another study (134).

We found no disturbances in the electrolyte balance in our patients as has been described after fasting (135) or intestinal bypass (119). Increased concentrations of uric acid as sometimes seen after fasting therapy, were not registered. On the contrary, uric acid levels decreased significantly. Variables reflecting liver function improved more than after fasting therapy (131), probably due to the greater weight reduction after surgery.

As could be expected, fasting blood glucose levels and the regulation of glucose metabolism improved significantly in parallel with a decrease in insulin levels, which is consistent with data obtained after conservative treatment of obesity (24). The significant correlations between body weight/ body fat reduction and blood glucose and plasma insulin and glucagon levels implicate that these improvements in carbohydrate metabolism are due to the reduction in body fat rather than to a low caloric

intake. The parallel decrease in blood glucose, plasma insulin and the improved glucose tolerance are well compatible with the view that these changes can be explained by an improvement of the poor insulin sensitivity of the large fat cells before treatment.

The lipoprotein profile improved after treatment and adopted a supposedly less atherogenic pattern. Plasma levels of triglyceride, cholesterol and LDL cholesterol decreased significantly and we found a moderate rise in plasma HDL concentrations. These alterations are also a known effect of weight reduction after conservative treatment (24) and was also noticed by Gleysteen and Barboriak (134), who used gastric bypass to achieve weight reduction. The positive changes in lipid metabolism are established six months after surgery. They were significantly correlated to the loss in body weight/body fat, indicating that the changes in lipid metabolism are due to the reduction in body weight/body fat rather than to the change in food intake. Other authors (24) also support the view that at least the elevations in HDL levels are caused by the weight loss as such and not by caloric restriction. Most of the variables involved in lipid metabolism were also correlated to the change in plasma insulin levels, indicating that the effects of body weight reduction on lipid metabolism may largely be mediated via insulin. In the present study the adipose tissue LPL activity was not clearly elevated and the mean enzyme activity in postheparin plasma was below the reference range. The lower LPL activities in this study compared to other investigations by our group (24, 50, 136) may be due to the weight reduction taking place immediately before surgery. However, these findings do not support the view that increased LPL activity in adipose tissue plays a primary role for the development of obesity (22).

In the present investigation we could not demonstrate the relationships between LPL activities and plasma triglyceride levels and HDL cholesterol concentrations, which might be expected from

current views of lipoprotein metabolism (137, 138). We believe that, in this particular situation, an influence of LPL on plasma triglyceride levels is masked by more marked changes in triglyceride secretion from the liver. Similarly, the effect of LPL on plasma HDL levels seems to be overridden by the significant changes in HL activity, which may be due to the decrease in plasma insulin levels.

5.2.5 Adipocyte heat production

Abnormalities in adipose tissue metabolism in obese individuals, such as increased LPL activity (22, 50, 98), decreased sensitivity to insulin (139, 140) and increased lipolysis (141), have been well documented. As all biochemical reactions in a cell lead to the dissipation of heat, the registration of cellular thermogenesis by microcalorimetry gives a quantitative measurement of total metabolic activity. This technique was used to further characterize the disturbed adipocyte metabolism in obese subjects. Our investigation confirmed a low adipocyte heat production in obese subjects (58). After weight reduction, however, heat production increased considerably and normalized, as expressed per cell. When expressed per g tissue, however, the heat production was still below that of control subjects. These data indicate that the decreased heat production found in adipocytes from obese individuals, as many other metabolic alterations, is a secondary phenomenon to the obese state rather than a primary pathogenic factor. Potentially, however, the reduced cellular heat production in obese subjects may represent a factor, which tends to perpetuate the obese state.

In an earlier report (58), we have found significant correlations between heat production and plasma insulin levels after moderate weight reduction and the same trends could be confirmed in this study. We could also register significant correlations between

alterations in different variables reflecting thyroid function and changes in heat production from adipocytes. These correlations were not found in our earlier investigation (58), probably because weight reduction and the alterations in thyroid function were less marked. The results of the present study, however, are consistent with our recent finding that hypothyroid patients have a clearly lowered adipocyte heat production, which normalizes upon treatment (142).

5.2.6 Prediction of weight loss.

In the literature body weight, resting metabolic rate, adipose tissue cellularity and T3 resin uptake test have been shown to be of predictive value for weight loss following dietary treatment of obesity (75). In the present investigation we found that these variables have no predictive value for the results of gastroplasty. Similarly, variables reflecting glucose metabolism, lipid transport and adipose tissue metabolism - all of which are frequently abnormal in obesity - were not related to postoperative weight loss. However, we could demonstrate that certain psychological features differentiated successful and unsuccessful patients with regard to weight reduction after surgery. Especially the combined signs of sensitivity and immaturity characterized the unsuccessful patients. These patients also had a significantly lower mean age, which is consonant with the more frequent signs of immature responses. Sensitive individuals often have difficulties to defend themselves against anxiety, which they sooner or later are liable to experience and it is possible that food and the act of eating serve anxiety curbing purposes to the sensitive patients. The use of alcohol (as a sedative?) was also more frequent among these patients. The psychological profiles of our patients were examined with rather sophisticated techniques. However, it is likely that similar information in clinical practice could be obtained by less cumbersome methods, such as a structured interview by a trained physician giving special emphasis to signs of sensitivity and immaturity.

SUMMARY

The etiology of obesity is still unknown, which is reflected by the numerous therapeutic alternatives currently available. For most grossly obese patients, surgical treatment seems to be the only realistic alternative to achieve permanent weight reduction. The increasing number of reports showing undesired metabolic side effects after intestinal shunts led to the development of gastric partitioning techniques. In the present investigation the gastroplasty procedure was evaluated as a means to achieve weight reduction in morbidly obese subjects. Our results can be summarized as follows:

1. The metabolic disturbances generally found in morbidly obese individuals could be confirmed. After weight reduction following gastroplasty, the metabolic pattern improved drastically. Cardiovascular risk factors such as hyperlipoproteinemia, hyperinsulinemia and glucose intolerance were eliminated or reduced. No adverse effects of gastroplasty could be demonstrated.
2. Psychologically, our obese group of patients were generally characterized by signs of immaturity. No gross deviations from average were found in their intellectual capacity. Signs of depression increased significantly after weight reduction. Depressive reactions were more prevalent in patients, who lost most weight.
3. The weight reduction after gastroplasty showed great interindividual variation (1-71 kg, 18 months after surgery) and was unsatisfactory (<20 %) in 1/3 of the patients. All patients with insufficient weight reduction developed dilations of the channel, i.e. the artificial pylorus created in the upper part of the stomach. Nearly 25 % of the patients with successful weight reduction also had dilation of their channel.

4. Severe immediate postoperative complications occurred in four patients (17 %). One patient suffered a lethal pulmonary embolus and another a high deep vein thrombosis, which was successfully removed by surgery. Two patients developed postoperative perforation in the upper part of the stomach. Early detection and immediate reoperation contributed to uneventful courses in both cases.

5. Basal as well as stimulated gastric acid secretion, which was above the reference range before surgery, decreased considerably after surgery. No morphologic changes in the gastric mucosa was seen postoperatively.

6. Comparison of data obtained before and after weight reduction gave no indications that any of the biochemical aberrations noted (especially adipose tissue lipoprotein lipase activity and adipocyte heat production) would represent a primary etiological factor for obesity in these patients.

7. Moderate decreases in levels of S-cobalamines, S-iron and B-folate, which in the long run may demand supplementation, occur after weight reduction following gastroplasty. This deficiency is probably due to the drastic reduction in food intake.

8. None of the morphometric or biochemical measurements (especially initial body weight, adipose tissue cellularity and thyroid hormone status) had predictive value for the weight loss registered after gastroplasty. However, the psychological profile recorded before surgery differentiated successful and unsuccessful patients with regard to weight reduction after gastroplasty.

7 CONCLUSIONS AND PERSPECTIVES

Treatment of obese patients is a demanding task and requires a long term commitment from both patient and physician. There is growing consent that overweight as such is not necessarily an indication for institution of a treatment programme. Instead therapy should be started when complications, such as orthopedic problems, hypertension or metabolic disturbances, arise as a consequence of the obese state. Similarly, a strong desire to reduce weight may be regarded as a psychological complication to obesity requiring treatment.

The selection of patients for different types of obesity treatment programmes often reflects attitude rather than decisions based on objective data. Conservative treatment is generally inexpensive, but although selection of patients for this treatment can be facilitated using certain biochemical parameters of predictive value (see above), the long term results are discouraging in the vast majority of patients. Surgical treatment is far more expensive, but the therapeutic results are more permanent, although failure rates of 30 - 40 % have been reported. Major complications to the surgical procedure and long term adverse effects may also occur. It is obvious that no surgical method is ideal and that all carry varying complications and side effects. However, this must be weighed against the social discomfort and the higher morbidity and mortality in patients with severe obesity.

The gastric procedures to treat morbid obesity were developed in order to eliminate the long term metabolic side effects seen after intestinal shunt surgery. The first alternative, the gastric bypass, is difficult to perform in morbidly obese patients and is followed by a high rate of early complications. The gastroplasty procedure is technically simpler and has a lower incidence of immediate postoperative complications.

Unfortunately, a long lasting weight reduction can not be guaranteed after this procedure and in fact about 1/3 of the patients do not loose weight satisfactorily. One factor determining weight loss after gastric surgery for obesity is the draining time from the upper pouch, which is related to the width of the draining channel (143). The resistance of the stoma in gastroplasty is evidently not sufficient and, especially in patients with pathological eating behaviour, dilation of the stoma may occur 6 - 8 months after surgery. Therefore this procedure can not be generally recommended until the problem with dilation of the draining channel has been successfully solved. A recent development within this field, the gastric banding procedure, seems to give a greater constancy of the draining channel and promising results have recently been published (144). It is of course critical that these new methods are extensively documented in a long term follow up, both with regard to clinical outcome and possible metabolic and other side effects.

Two current theories on the etiology of obesity have been discussed in the present investigation; the LPL theory and the existence of an increased metabolic efficiency in obese subjects (as measured by microcalorimetry). Our data do not support the view that these metabolic alterations among obese individuals are primary defects, contributing to the development of obesity. However, obesity is certainly not one pathophysiological entity, but comprises several aberrations sharing the same symptomatology. Group mean values in non-selected groups of obese patients, therefore, may be of limited relevance for the various etiological subgroups. A more fruitful approach to study etiological mechanisms for the development of obesity may be to divide patients into more homogenous groups, using certain biochemical, psychological or clinical variables and then compare differences and similarities in other variables, which may be of etiological significance. Such a grouping of morbidly obese patients might also help us to assign patients for an optimal treatment programme.

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10 APPENDIX

Papers I - V.

GASTROPLASTY AS A TREATMENT FOR MASSIVE OBESITY - A CLINICAL AND
BIOCHEMICAL EVALUATION

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ABSTRACT

Twenty-four grossly obese patients were operated upon with horizontal gastroplasty. One patient died postoperatively from pulmonary embolism. The remaining 23 were extensively studied before and repeatedly after surgery. Eighteen months postoperatively the average weight loss was 34,4 kg (range 1-71 kg). Seven patients had a weight reduction of less than 20 % after 18 months.

Postoperatively, biochemical variables reflecting glucose and lipid metabolism and liver function improved. B-hemoglobin, S-iron levels as well as serum concentrations of folate and cobalamines decreased significantly. No negative histological changes could be found in the gastric mucosa during the follow-up period. Although only positive metabolic changes have been registered, we feel that gastroplasty, which is not without early postoperative complications, and has a failure rate of about 30 %, cannot be generally recommended until the problem with postoperative dilation of the stoma has been successfully solved.

Key words: Obesity; gastroplasty; weight reduction.

INTRODUCTION

Gastric bypass was introduced in 1966 by Mason as an alternative to jejunoileal bypass operations in the treatment of severe obesity. The gastric procedure did not lead to any of the serious metabolic complications seen as the result of the blind loop syndrome created in the jejunoileal bypass operation. However, it soon became evident that the overall mortality rate did not differ between the two methods; patients lost after gastric by-pass died in the early postoperative phase due to surgical technical complications (1), while fatal complications in patients operated with jejunoileal bypass occurred months to years later due to metabolic disturbances (2). In order to overcome the surgical problems associated with gastric bypass operations a number of modifications of the original operation have been developed (3,4,5).

In this study we have employed one of the earliest modifications, the horizontal gastroplasty introduced by Gomez (6). A small upper pouch is created by applying a horizontal staple line across the stomach leaving a narrow opening along the greater curvature. The initial report by Gomez (6,7) showed few postoperative complications and a weight loss comparable to that after gastric bypass. Although severe metabolic disturbances such as short bowel and blind loop syndrome complications do not occur after gastric procedures for obesity, the operations do conceivably lead to profound alterations in nutritional pattern and upper gastrointestinal physiology. However, the short and long term metabolic effects of these operations have so far been poorly documented. The present report is a follow up study on alterations in gastrointestinal function and various biochemical variables in 23 patients after gastroplasty.

MATERIAL AND METHODS

Patients

Patients above 50 years of age or with a history of cardiovascular disease, severe diabetes demanding insulin treatment or previous psychiatric disorders including known alcoholism were not considered eligible for surgery. All the 23 patients (19 women and 4 men between the ages of 23 and 44) operated in 1979 - 1980 were included in the study.

Before surgery the patients were encouraged to reduce weight. The lightest patient managed to reduce her weight from 110 to 93 kg and the heaviest patient from 220 to 192 kg. The mean weight reduction before surgery was 4 kg (0-28 kg). At operation the mean body weight was 128 kg (93-192 kg) and the mean Broca's index* was 2,1 (1,6-3,2).

Surgery and follow-up

All patients were operated upon by the same team essentially using the technique (8) described by Gomez (7) (fig 1).

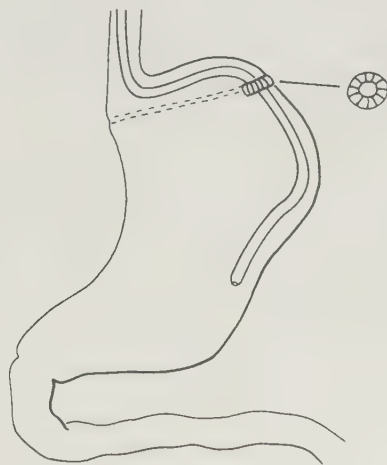


Fig I Completed gastroplasty

$$\text{*Broca's index} = \frac{\text{body weight (kg)}}{\text{height (cm)} - 100}$$

Antibiotic prophylaxis with doxycycline and anti-thrombotic prophylaxis with Macrodex^R was given. Intensive care was not required. Postoperatively parenteral nutrition and cimetidine was given for 3 days; thereafter the patients received a liquid diet followed by purée diet after one week. At dismissal the patients were instructed to avoid whole meat, vegetables of threadlike structure and to take frequent small meals and to drink between meals. The routine postoperative follow-up included a monthly visit for the first 3 months and a visit every 3 months thereafter. One patient died (see below) and our two first patients were only followed with regard to weight reduction and clinical parameters. The remaining 21 patients underwent an extensive clinical and metabolic investigation in the ward before surgery and 6 to 8 months after the operation. Additionally 13 of the patients with the largest weight reduction had the metabolic follow-up examination repeated 12 - 18 months after surgery. Gastroesophageal morphology was evaluated on at least 3 occasions.

Gastric morphology

Gastrosocopy (P2 gastroscope, Olympus, diameter 7 mm) was carried out by a surgeon from the operating team and included biopsies from the distal oesophagus, cardia and antrum. Upper G-I series was performed according to routine procedures.

Channel dilation was considered to have occurred if its width was twice that of the gastroscope diameter. In these patients, the upper pouch was immediately emptied of contrast medium during the upper G-I series. Dilation of the pouch was estimated by evaluation of the gastrosocopy and x-ray results. Oesophageal manometry including reflux provocation was carried out according to Sandmark (9) before and 6 - 12 months after surgery.

Laboratory investigations

Basal and stimulated gastric acid secretion were studied pre- and postoperatively using a pentagastrin load (6 μ g/kg body weight) to stimulate gastric acid secretion. After surgery the nasogastric tube for the sampling was applied into correct position with the aid of a leader under x-ray guidance. Hematologic data, S-kreatinin, S-iron, S-TIBC, S-ferritin, S-gastrin, electrolytes, minerals, uric acid and variables reflecting liver function were determined according to routine techniques in our laboratory. Tyroxin (T4) was measured with a competitive binding protein technique (10). Insulin, glucagon, triiodothyronine (T3) and reverse triiodothyronine (rT3) were measured by radioimmunoassay. P-triglyceride and P-cholesterol were determined by enzymatic methods (11,12). P-HDL, P-LDL cholesterol, body fat and lean body mass was measured as described earlier (13).

Statistical methods

Differences between groups were evaluated using Wilcoxon's rank order test for paired observations.

RESULTS

Clinical observations

The patients reported a feeling of satiety after their small meals and they did not feel severe hunger in spite of low daily caloric intake. During the first month after surgery, before adjusting their food intake, several patients had a tendency to vomit. In 2 patients, frequent prolonged vomiting led to swelling of the channel causing temporary gastric retention. They required short readmission to the hospital for intravenous fluids due to hypocalcemic metabolic alkalosis. Endoscopic or surgical intervention was never required. Two patients became pregnant 9 - 12

months following surgery. The pregnancies were well tolerated and free of complications.

Early surgical complications

One patient died in a massive pulmonary embolus about 20 hours after surgery; in this case a cholecystectomy was also performed. Two patients had to be reoperated and drained because of leakage from the upper pouch 2 and 3 days after surgery. They both had uneventful postoperative courses. Two accidental splenectomies were performed. One patient developed a deep iliac vein thrombosis on the 3rd postoperative day, which was surgically removed.

Late surgical complications

The frequency of verified staple line ruptures/dilation of the channel or dilation of the upper pouch are shown in Table I. Most of the channel dilations following staple line ruptures were demonstrated at the second check-up about 12 months after surgery and the patients could often tell at what time they had been able to eat with less restrictions than before (4 - 10 months after surgery).

Table I Distribution of late postoperative complications and average position in operation series in patients with differential weight loss 18 months after surgery.

	Body weight loss in % compared to body weight at surgery		
	> 40	20-40	< 20
Number of patients	4	12	7
Average position	10.2	10.4	9.4
Enlarged channel	2	3	7
Enlarged pouch	2	1	0

The weight reduction and the frequency of late surgical complications were similar in patients operated early and late in the series (average position in Table I). It should be pointed out that also some patients with verified staple line rupture/channel dilation lost weight successfully; 5 patients with dilation of the channel had a weight reduction exceeding 20 % 18 months after surgery.

Weight loss

The average weight loss (preoperative weight loss excluded) of the entire group (n=23) is shown in Figure 2 as well as the change in lean body mass and body fat.

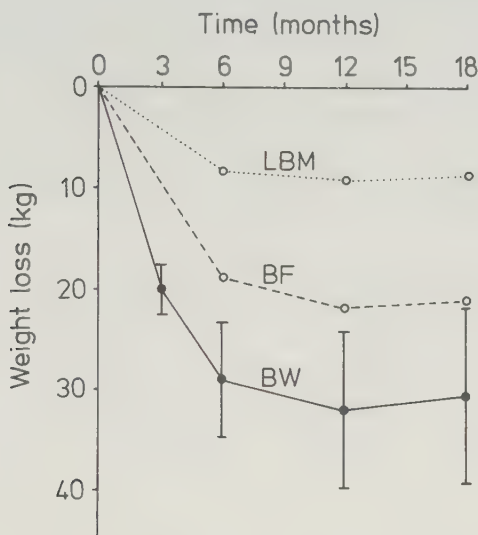


Fig II Reduction in body weight (BW), lean body mass (LBM) and body fat (BF) (mean $\pm$ SD) in 23 obese subjects after gastroplasty operation (preoperative weight reduction not included). At operation the initial weight was 128 $\pm$ 21 kg. The mean weight reduction before surgery was 4 kg (0 - 28 kg).

The initial weight loss was rapid and 6 months after the operation the mean weight loss was 33 kg (range 12 - 53 kg); 70 % could be accounted for by a loss in body fat. Eighteen months postoperatively we found a mean weight loss of 34,4 kg (range 1-72 kg). After an initial substantial weight loss 3 patients started regaining weight 6 months after surgery. Eighteen months after surgery 2 of them had regained their preoperative weight. In total about 30 % of the patients had unsatisfactory weight reduction (less than 20 % weight reduction after 18 months).

Biochemical variables

The different biochemical variables analyzed before and at follow-up 6 to 8 months after surgery are shown in Table II - IV. B-hemoglobin (Table II) decreased by about 5 %, but none of our patients developed an anemia during the follow-up period. S-iron concentrations decreased significantly in parallel with S-ferritin levels. In 3 patients S-iron levels were reduced below 10 $\mu\text{mol/l}$. Also S-cobalamine and S-folate levels decreased markedly and 6 patients had B-folate concentrations below the lower reference limit.

Except for a transient hypokalemia in two patients suffering from prolonged vomiting 2 - 3 months after surgery (see above) serum levels of sodium, potassium and calcium were essentially unchanged. There was a significant reduction in S-magnesium levels, although none of the patients developed hypomagnesemia. One of the vomiting patients developed a transient hyperuricemia, but at follow-up there were no signs of hyperuricemia for the group as a whole.

Preoperatively, variables reflecting liver function (Table III) were frequently above the reference range; they improved considerably at follow-up. In fact nearly 1/3 of the patients had one or more variables above the reference range before operation compared to none at follow-up.

Table II Haematologic data before gastroplasty (I) and at follow-up 6-8 months postoperatively (II). Data are given as mean $\pm$ SD.

Variable	Reference range	I	II	I vs. II
B-hemoglobin	115-163	142.4 $\pm$ 13.4	135.6 $\pm$ 15.9	p<0.05
B-erythrocyte count, no./l	3.7-5.4 $\times 10^{12}$	4.75 $\pm$ 0.37	4.61 $\pm$ 0.41	p<0.05
B-erythrocyte volume fraction, %	37-49	41.6 $\pm$ 3.8	39.9 $\pm$ 4.6	p<0.05
S-iron, μ mol/l	10-30	23.4 $\pm$ 7.6	18.9 $\pm$ 8.7	p<0.05
S-ferritin, μ g/l	>10	48 $\pm$ 55	31 $\pm$ 33	p<0.05
S-cobalamines, pmol/l	110-650	372 $\pm$ 105	282 $\pm$ 125	p<0.005
B-folate, nmol/l	70-200	138 $\pm$ 45	75 $\pm$ 29	p<0.005

Table III Variables reflecting liver function before gastroplasty (I) and at follow-up 6-8 months postoperatively (II). Data are given as mean $\pm$ SD.

Variable	Reference range	I	II	I vs. II
S-bilirubin (total), μ mol/l	3-20	13.6 $\pm$ 3.6	10.6 $\pm$ 4.6	p<0.01
S-alkaline phosphatase activity, μ kat/l	0.8-4.6	3.37 $\pm$ 0.75	2.7 $\pm$ 0.56	p<0.005
S- γ -glutamyl transferase activity, μ kat/l	<1.0	0.52 $\pm$ 0.56	0.29 $\pm$ 0.16	p<0.025
S-asparagine aminotransferase activity, μ kat/l	<0.67	0.67 $\pm$ 0.66	0.39 $\pm$ 0.18	p<0.025
S-alanine aminotransferase activity, μ kat/l	<0.67	0.73 $\pm$ 0.79	0.27 $\pm$ 0.23	p<0.005

Five patients had a hypertriglyceridemia (2,4 - 5,3 mmol/l) before surgery (Table IV). All but one normalized postoperatively. In fact triglyceride levels decreased postoperatively in all patients. The triglyceride reduction was most prominent in patients with the greatest weight reduction. The significant decrease in P-cholesterol was fully accounted for by a fall in LDL cholesterol concentrations, whereas the rise in HDL levels did not reach statistical significance. The LDL/HDL ratio changed from 3,8 to 3,0 postoperatively.

Variables reflecting thyroid function did not change significantly. As discussed more in detail elsewhere (9) the decrease in S-thyroxine concentration could almost entirely be attributed to the patients showing the greatest weight loss. Similarly, the decrease in blood glucose, plasma insulin and glucagon levels was most prominent in patients with considerable weight reduction (Table IV). Five patients with high levels of plasma insulin (above 30 u/ml) normalized after surgery and three patients with high levels of plasma glucagone (above 250 g/ml) before operation almost normalized postoperatively.

Table IV Variables reflecting lipid and glucose metabolism before gastroplasty (I) and at follow-up 6-8 months postoperatively (II). Data are given as mean $\pm$ SD.

Variable	Reference range	I	II	I vs. II
P-triglyceride, mmol/l	0.3-2.1	1.9 $\pm$ 1.2	1.3 $\pm$ 0.8	p $\leq$ 0.005
P-cholesterol, mmol/l	3.2-7.2	5.6 $\pm$ 1.1	5.0 $\pm$ 1.0	p $\leq$ 0.01
P-HDL cholesterol, mmol/l	0.8-1.7	0.96 $\pm$ 0.20	1.03 $\pm$ 0.31	n.s.
P-LDL cholesterol, mmol/l	1.3-4.5	3.66 $\pm$ 1.06	3.10 $\pm$ 1.15	p $\leq$ 0.025
LDL/HDL ratio	<3.5	3.9 $\pm$ 1.5	3.2 $\pm$ 1.8	p $\leq$ 0.025
B-glucose, mmol/l	3.3-5.6	6.3 $\pm$ 2.3	4.5 $\pm$ 0.6	p $\leq$ 0.005
P-insulin, μ U/ml	5-25	21.6 $\pm$ 17.2	9.5 $\pm$ 6.5	p $\leq$ 0.025
P-glucagon, μ g/ml	50-250	193 $\pm$ 94	119 $\pm$ 89	p $\leq$ 0.025

Gastric acid secretion and morphology

80 % of the patients had an elevated stimulated gastric acid secretion preoperatively (above 20,9 mmol/h for women and 26,1 mmol/h for men). Thirty per cent also had an increased basal acid secretion (above 3 mmol/h for women and 4 mmol/h for men). At endoscopy 1/3 of the patients had a minor gastritis, which was confirmed by histology from the gastric mucosa. Postoperatively the high acid secretion decreased in all patients except 2. At endoscopy after surgery there were no visual or histological signs of more severe gastritis than before the operation. The serum levels of gastrin remained within the normal preoperative range. Oesophageal manometry including reflux provocation was normal and did not change after surgery.

DISCUSSION

The gastroplasty operation has been widely used as a therapeutic procedure for severe obesity during the last decade. Although gastroplasty is easier to perform than for example gastric bypass, it is not without complications. The early surgical complications, especially perforation of the upper pouch, are serious and well known from the literature (1,14) and in our series we have two such cases. These leakages are mostly unpredictable. Pouch ischemia or an improperly placed nasogastric tube might be the causes of some of these perforations. Early detection using clinical parameters and immediate reoperation and drainage, including the use of a Witzel fistula, contributed to an uneventful course in our two patients.

From the literature it is evident that weight reduction is less after gastroplasty compared to gastric bypass (15,16). A number of new methods such as vertical banded gastroplasty by Mason (4) and gastric banding have been introduced to overcome the problem with dilation of the pouch

and channel in horizontal gastroplasty, but no method has yet been shown to be comparable to gastric bypass in a long term follow up. The failure rate (less than 20 % weight loss after 18 months) in our material was almost 30 %, which has also been reported in recent communications (16,17).

It is important to point out that the validity of any long term results concerning weight reduction is greatly influenced by the number of patients reporting at follow up; patients lost to follow up should be classed as failures (18,19). Many failures may be explained by late surgical complications, such as enlargement of the pouch, staple line rupture or rupture of the Prolene suture leading to dilation of the channel. We could find no technical surgical explanation to the high incidence of channel dilations in this series. We believe that other reports may underestimate the frequency of this late surgical complication unless all patients, even those who lose weight successfully, are followed with postoperative gastroscopy or an adequate upper G-I series, as we found 5 cases with adequate weight reduction in spite of channel dilation. Obviously these patients had a good initial weight reduction, which may have been the incitement to adopt new eating habits.

A major difference between gastric bypass and gastroplasty is the fact that food is bypassed from the greater curvature of the stomach in gastric bypass, creating a situation similar to that after a Billroth II operation. Experimental data (20) have demonstrated that gastric bypass reduces serum gastrin levels, which may interfere with satiety, and reduces secretion of pancreatic exocrine enzymes, which may have an impact on food absorption. We also know that patients operated on by gastric bypass have a reduced pancreatic polypeptide secretion (21). The different weight reduction results from gastric bypass and gastroplasty may therefore be due not only to surgical technical factors but also to these highly different effects on gastrointestinal physiology.

The biochemical alterations following weight reduction after bariatric surgery may be related to changes in body compartments or consequences of the drastically reduced food intake. Most of the biochemical consequences after weight reduction seem to be favourable regardless the method used to achieve weight reduction. The gastroplasty procedure could at least theoretically lead to disturbances in gastric acid secretion or gastric morphology. In this study no such negative changes were found. On the contrary the basal as well as the stimulated acid secretion decreased in most patients, probably due to the fact that their gastric volume was above average before gastroplasty with a corresponding increase in the amount of parietal cells. After surgery the stomach was not stimulated by a large food intake and consequently parietal cell mass may be reduced.

Most of the biochemical alterations recorded after gastroplasty must be regarded as beneficial to the patients. Some of the side effects registered, such as low levels of S-cobalamines, S-iron and B-folat, are most likely due to the drastically reduced food intake. However, no anemia or neuropathy was registered, probably because the patients were given supplementation when their deficiency was detected. We found no disturbances in the electrolyte balance in our patients as has been described after fasting (22) or intestinal bypass (2). Increased concentrations of uric acid sometimes seen after fasting therapy were not registered. In fact uric acid levels decreased significantly. Variables reflecting liver function improved more than after fasting therapy (13), probably due to the greater weight reduction after surgery. Also the impaired glucose and lipid metabolism seen in obese patients improved considerably, as is the case after conservative treatment (13). The LDL/HDL ratio and blood glucose levels were significantly reduced after surgery, thereby reducing the risk of cardiovascular complications, which are common among these patients (23).

Apparently no severe metabolic disturbances occur after gastroplasty as is the case after intestinal bypass. In fact most metabolic changes are

favourable. However, it cannot be excluded that these patients, due to a reduced food intake, may in the long run suffer from iron, vitamin and trace element deficiencies as indicated in this and another study (19). Also, this procedure frequently gives unsatisfactory weight reduction and although factors of predictive value may exist (8), we feel that gastropasty should be used restrictively until the problem with postoperative dilation of the stoma has been successfully solved.

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EFFECTS OF WEIGHT REDUCTION AFTER GASTROPLASTY ON GLUCOSE AND LIPID METABOLISM.

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ABSTRACT

We have studied effects of weight reduction after gastroplasty on glucose and lipid metabolism in 15 grossly obese subjects. Their body weight decreased from 127 ± 13 kg to 97 ± 14 kg 6 months after surgery and remained essentially stable 8 months later. There was a marked improvement of lipid and carbohydrate metabolism with significant reductions in blood glucose, plasma insulin and glucagon levels and in glucose tolerance. LPL activity in adipose tissue was in the upper reference range and LPL activity in postheparin plasma tended to be low. Plasma triglyceride, cholesterol and LDL cholesterol concentrations decreased significantly, while HDL cholesterol levels tended to rise. Concomitantly, there was an increase in triglyceride clearance rate. Most of these changes were significantly correlated to the reduction in body weight/body fat, indicating that the metabolic improvements are due to body fat reduction as such.

Key words: Obesity, HDL cholesterol, LDL cholesterol, insulin, glucagon, body fat.

INTRODUCTION

Obesity is associated with an increased risk for coronary heart disease (1). In moderate obesity, the increased risk seems mainly to be due to alterations in endocrine pancreatic function, adipose tissue metabolism, and glucose and lipid transport. Massive obesity, in addition, represents an independent risk factor (2).

The increased insulin concentrations in obese individuals seem to be the consequence of an impaired hepatic extraction of insulin (3,4) in combination with an enhanced secretion (5), and are often accompanied by a decreased peripheral insulin sensitivity (6). Studies on basal and stimulated levels of glucagon have however led to conflicting results (7,8,9,10). The plasma lipoprotein pattern often demonstrates increased VLDL levels due to increased hepatic secretion of triglycerides (3,11,12). Also adipose tissue lipoprotein lipase activity (LPL) is increased (3,13,14,15,16) and its regulation impaired (3,16,17). Most of the alterations in glucose and lipid metabolism seem to ameliorate on weight reduction (7,12), indicating that these alterations are consequences rather than causes of obesity.

The beneficial effects of weight reduction by caloric restriction are well documented (3,12). It is also well known that intestinal by-pass surgery leads to a marked improvement in serum cholesterol levels (18), thereby reducing one of the risk factors involved. However, due to inadequate weight reduction after fasting and undesired long-term metabolic alterations after intestinal by-pass the use of gastric surgery to control morbid obesity has increased. Recent studies have reported favourable changes in plasma lipoprotein concentrations (19) following weight loss induced by different gastric procedures.

The aim of the present investigation was to describe the effect of a large and rapid weight reduction after gastroplasty on glucose and lipid

metabolism and to study the relationship between the expected metabolic improvements and the loss in body weight/body fat.

MATERIAL AND METHODS

Patients and experimental design

Fifteen patients, 12 women and 3 men, between the ages of 23 and 41, participated in the study, which was approved by the departemental ethics group. They all had a long history of overweight and documentation of trial at weight reduction with conservative methods. The patients selected for the study came spontaneously to the surgical out patient clinic or were referred there because of severe obesity. High age (above 50), history of cardiovascular disease, severe diabetes demanding insulin treatment, and previous psychiatric disorder as well as known alcoholism, were considered contraindications for surgery. None showed signs of severe metabolic or endocrine disease. Three patients had chemical diabetes, as defined by fasting glucose levels above 7 mmol/l, 5 patients had a hypertriglyceridemia (2,4 - 5,3 mmol/l) and 2 patients had a slight increase in plasma-cholesterol concentrations (7,5 - 7,6 mmol/l). The patients were operated 1979-1980 by the same operating team, using a slight modification (20) of the operative technique described by Gomez (21). A complete metabolic investigation was performed in all patients under standardized conditions in the ward before surgery, 6 - 8 months after surgery and in most patients 12 - 18 months postoperatively. The initial body weight at operation ranged from 112 - 158 kg; the body weight after 6 and 12 months 82 - 135 kg and 75 - 135 kg respectively (Table I). Mean body weight 12 months after surgery was 93,6 kg ($\pm$ 17,4 kg).

Body compartments and fat cell size

Total body ^{40}K was determined by a whole body scanner calibrated with a

phantom. Lean body mass and body fat were estimated according to Forbes (22). Cell size was determined by microscopic examination of adipocytes prepared by collagenase treatment of adipose tissue (20).

Plasma lipids and lipoproteins

HDL cholesterol was determined in the clear supernatant obtained after precipitation of VLDL and LDL by $MgCl$ and dextran sulphate (23). Triglyceride and cholesterol were determined by enzymatic methods (24,25). LDL cholesterol was calculated according to the formula $LDL\ cholesterol = plasma\ cholesterol - (HDL\ cholesterol + 0,45 \times plasma\ triglyceride)$ (modified to SI units from 26).

Assays for lipolytic enzymes

LPL activity in adipose tissue was determined in surgical biopsies of gluteal fat after elution with heparin (27,28). The substrate was a trioleylglycerol emulsion stabilized by lysolecithin (29); released fatty acid was separated by liquid-liquid partition (30). LPL activity in adipose tissue was related to tissue weight and also expressed per cell. LPL and hepatic lipase (HL) activities were determined in postheparin plasma drawn 10 min after the injection of 50 U heparin/kg body weight, with methods described earlier (29). One mU of enzyme activity represents the release of 1 nmol fatty acid per min.

Glucose and lipid load

Glucose tolerance was estimated from an intravenous glucose load using 50 g glucose/ m^2 body surface. Intravenous administration was used as many of the patients postoperatively may have had difficulties in swallowing the necessary amount of glucose solution during the stipulated time. Blood glucose was measured by the glucose - oxidase method. Plasma insulin (31) and glucagon (32) were determined by radioimmunoassay. The

intravenous fat tolerance test (IVFTT) was performed as described by Carlsson & Rössner (33).

Statistical evaluations

Differences between preoperative values and values obtained at follow up were evaluated using Wilcoxon's rank order test for paired observations. Correlations between different metabolic variables were calculated using Spearman's rank correlation test. The experimental data have been compared to the reference ranges routinely used at the laboratory or, when indicated, to a control group of twenty normal weight individuals matched for age and sex.

RESULTS

Weight reduction

The mean body weight reduction at follow up after 6 months was 24 % (range 12 - 34%) compared to body weight at surgery. Nearly 70 % of the weight reduction could be accounted for by a loss in body fat (Table I). The decrease in fat cell size was highly significant (Table I) and as could be expected highly correlated to the decrease in body fat ($P \leq 0,01$).

Table I Body compartments and fat cell size before gastroplasty (I) and at follow-up 6-8 months postoperatively (II). Data are given as mean $\pm$ SD:

*) Reference values 0.24-0.52 μ g lipid per cell. †) I vs II $p \leq 0.005$.

	I	II
Body weight (kg)	127 $\pm$ 13	97 $\pm$ 14
Body fat (kg)	73 $\pm$ 13	52 $\pm$ 8
Lean body mass (kg)	54 $\pm$ 9	45 $\pm$ 9
*) Fat cell size †)	0.639 $\pm$ 0.13	0.430 $\pm$ 0.08

At follow up 18 months after surgery body weight was 94 ± 17 kg representing a mean body weight reduction of 27 % compared to body weight at surgery; i.e. most of the weight reduction occurred during the first 6 months following surgery.

Plasma lipids and lipoproteins

Changes in plasma lipids and lipoproteins are shown in Table II. Before surgery 5 patients had a hypertriglyceridemia between 2,4 - 5,3 mmol/l. All but one normalized postoperatively and in fact triglyceride levels decreased postoperatively in all patients. The mean reduction in plasma triglyceride concentration was about 30 % and 18 months postoperatively the plasma triglyceride concentrations showed a slight further improvement ($1,2 \pm 0,4$ mmol/l).

A 12 % significant decrease in plasma cholesterol levels was registered and maintained at least 18 months after surgery ($4,9 \pm 0,8$ mmol/l). In fact cholesterol levels decreased postoperatively in all but one patient. The fall in plasma cholesterol levels could be entirely accounted for by a decrease in plasma LDL levels. The moderate rise in HDL cholesterol levels did not reach statistical significance but was maintained at the 18 months follow up ($1,08 \pm 0,22$ mmol/l). The LDL/HDL ratio decreased by 18 % 6 months after surgery.

Table II. Plasma lipids, HDL and LDL concentrations, and LDL/HDL ratio before gastroplasty (I) and at follow-up 6-8 months postoperatively (II). Data are given as mean $\pm$ SD.

	Normal range	I	II	I vs II
P-cholesterol (mmol/l)	3.2 - 7.2	5.6 ± 1.1	5.0 ± 1.0	$p \leq 0.01$
P-triglyceride (mmol/l)	0.3 - 2.1	1.9 ± 1.2	1.3 ± 0.8	$p \leq 0.005$
P-HDL-cholesterol (mmol/l)	0.8 - 1.7	0.95 ± 0.20	1.02 ± 0.30	ns
P-LDL-cholesterol (mmol/l)	1.3 - 4.5	3.68 ± 1.06	3.12 ± 1.15	$p \leq 0.025$
LDL/HDL ratio	< 3.50	3.87 ± 1.48	3.18 ± 1.78	$p \leq 0.025$

LPL activities and lipid load

Alterations in postheparin lipoprotein lipase activity, hepatic lipase activity and IVFTT are shown in Table III.

The mean LPL activity of adipose tissue was normal when related to tissue weight and in the upper reference range when expressed as enzyme activity per cell. For technical reasons only an insufficient number of data, which did not allow statistical evaluation, were available at follow up.

The mean activity of LPL in postheparin plasma was below the reference range and decreased postoperatively although the decrease did not reach statistical significance. The activity of HL in postheparin plasma was elevated in 2 patients before and after weight reduction. The HL activity decreased after weight reduction by 27 %, which was highly significant.

The elimination rate of exogenous triglyceride (IVFTT) was normal in all patients; however a highly significant increase was found after weight reduction. The well known inverse relation between K_2 values and plasma triglyceride concentration (33) was obvious before treatment ($r = -0,72$, $P \leq 0,005$) and remained after weight reduction ($r = -0,60$, $P \leq 0,025$).

Glucose metabolism

Variables reflecting glucose metabolism are shown in Table IV and in fig 1 - 3.

The mean fasting blood glucose levels were increased before surgery and decreased significantly at follow up. Two patients had fasting blood glucose levels above 7 mmol/l before surgery compared to none at follow up 6 and 18 months after surgery. There was a significant reduction in insulin levels after treatment and the five subjects with overt hyperin-

Table III. Lipoprotein lipase activity, hepatic lipase activity and IVFTT before gastroplasty (I) and at follow-up 6-8 months postoperatively (II). Data are given as mean $\pm$ SEM.

	Reference values	I	II	I vs II
Postheparin plasma LPL activity (mU/ml)	70 - 145	61.9 $\pm$ 5.00	52.9 $\pm$ 4.16	ns
Postheparin plasma HL activity (mU/ml)	320 - 620	498 $\pm$ 53.1	364 $\pm$ 63.7	p $\leq$ 0.005
IVFTT: k ₂ value (% per min)	2.2 - 7.4	4.77 $\pm$ 0.43	6.12 $\pm$ 0.49	p $\leq$ 0.005
Adipose tissue LPL activity (mU/g tissue)	5.2 - 14.8	6.6 $\pm$ 1.6		
Adipose tissue LPL activity (mU/10 ⁶ cells)	2.1 - 5.9	4.2 $\pm$ 1.0		

Table IV. Glucose, insulin and glucagon before gastroplasty (I) and at follow-up 6-8 months postoperatively (II). Data are given as mean $\pm$ SEM.

	Reference values	I	II	I vs II
B-glucose (mmol/l)	3.3 - 5.6	5.9 $\pm$ 0.53	4.6 $\pm$ 0.20	p $\leq$ 0.005
P-insulin (μ U/ml)	5 - 25	19 $\pm$ 4.5	9.3 $\pm$ 1.8	p $\leq$ 0.025
P-glucagon (μ g/ml)	50 - 250	188 $\pm$ 17	106 $\pm$ 22	p $\leq$ 0.025

sulinemia before treatment normalized following surgery. Similarly, mean plasma glucagon concentrations were in the upper part of the normal range before treatment and decreased significantly after surgery. Three of our patients had increased fasting glucagon concentrations before weight reduction; one was normalized after treatment.

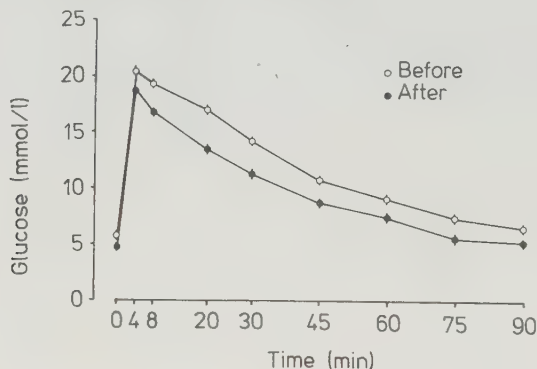


Fig 1 Blood glucose levels during an intravenous glucose load before gastroplasty and at follow up 6 - 8 months postoperatively. Data are given as mean $\pm$ SEM.

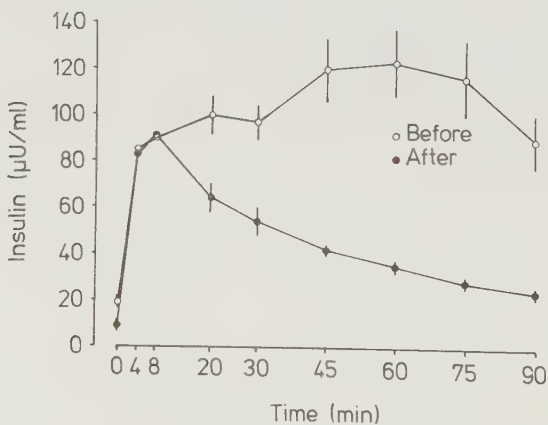
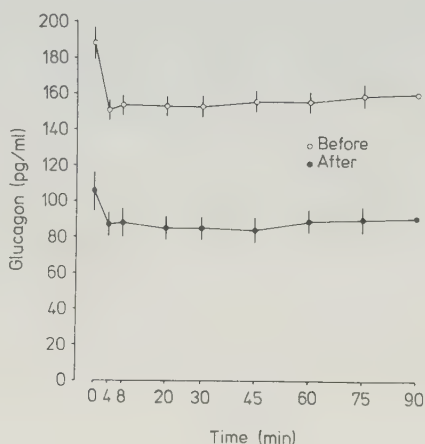


Fig 2 Serum insulin levels during an intravenous glucose load before gastroplasty and at follow up 6 - 8 months postoperatively. Data are given as mean $\pm$ SEM.

As seen in fig 1, 2 and 3 the blood glucose pattern as well as plasma insulin and plasma glucagon pattern improved significantly after weight reduction. The considerable improvements in carbohydrate metabolism were found to be significant also when the patients with chemical diabetes before surgery were excluded from the statistical evaluations.

Fig 3 Plasma glucagon levels during an intravenous glucose load before gastroplasty and at follow up 6 - 8 months post-operatively. Data are given as mean $\pm$ SEM.



Correlations

As mentioned above 90 % of the weight reduction took place during the first 6 - 8 months among the majority of the patients. As could be expected the decrease in cell size (Table I) was significantly correlated to the decrease in total body fat ($P \leq 0,025$) and cell size before treatment was also significantly correlated to total body fat ($p \leq 0,025$). The reduction in body weight was significantly correlated with the decrease in levels of plasma insulin ($P \leq 0,05$), hepatic lipase activity in post heparin plasma ($P \leq 0,05$), blood glucose ($P \leq 0,05$), plasma cholesterol ($P \leq 0,05$) plasma triglyceride ($P \leq 0,05$), and to the increase in plasma

HDL cholesterol ($P \leq 0,025$); essentially the same relationships were found if the correlations were made to the reduction in body fat.

As could be expected the decrease in plasma levels of insulin (Table IV) was significantly related to the reduction in levels of blood glucose ($P \leq 0,025$) and plasma glucagon ($P \leq 0,05$), but not to the changes in plasma protein concentrations. The decreased plasma levels of glucagon after weight reduction (Table IV) could not be statistically correlated to any of the biochemical variables involved in lipid metabolism.

The changes in of lipoprotein lipase and hepatic lipase activities in postheparin plasma (Table III) were not significantly correlated with alterations in any of the plasma lipoprotein fractions.

DISCUSSION

Obesity is associated with an increased mortality rate (34,2), especially if the overweight is great, and augments the risk to develop diabetes, arteriosclerosis and coronary heart disease (1). The risk factors for the development of these diseases, such as hyperlipoproteinemia and hyperglucosemia, are well known metabolic concomitants to obesity; therefore an ideal method to achieve weight reduction should also reduce the biochemical and metabolic abnormalities associated with obesity without causing additional metabolic disturbances. It is generally assumed, that the changes in lipid and glucose metabolism are consequences of the obese state or of the augmented food intake among obese individuals. However, some authors (35) claim that disturbances in the LPL activity in adipose tissue may play a primary role for the development of obesity.

In the present study we have monitored the effects of a rapid and large weight reduction achieved after gastroplasty in 15 grossly obese patients on some aspects of glucose and lipid metabolism. After surgery the pa-

tients were forced to restrict their food intake, leading to a rapid weight reduction and improvement of many metabolic abnormalities. Even if the weight loss and also the metabolic changes varied considerably, it should be pointed out that almost all patients were overweight also at the follow-ups after surgery.

As could be expected, glucose metabolism improved significantly after weight reduction, which is consistent with data available in other reports (12,19). The close relationships between body fat reduction and blood glucose and plasma insulin and glucagon levels imply that these improvements in carbohydrate metabolism are due to the reduction in body fat rather than to a low caloric intake, which is consistent with the pattern found in patients studied in caloric steady state before and after weight reduction (7). The parallel decrease in blood glucose, plasma insulin and the improved glucose tolerance are well compatible with the view that these changes can be explained by an improvement of the poor insulin sensitivity of the large fat cells before treatment (6,36).

The plasma lipoprotein pattern demonstrated a significant decrease in plasma triglyceride, cholesterol and LDL concentrations and a moderate rise, although not statistically significant, in HDL concentrations, which was maintained also 18 months following surgery. This is a well-known effect of weight reduction with conservative treatment (7) and was also noted by Glyesteen and Baboriak (19) who used gastric by-pass to achieve weight reduction. In our patients, the cardiovascular risk index, LDL cholesterol/HDL cholesterol decreased by about 20 %. The positive alterations in lipid metabolism were established 6 months after surgery. They were significantly correlated to the loss in body weight/body fat, indicating that the changes in lipid metabolism are due to the reduction in body weight/body fat rather than to the change in food intake. In analogy with our results obtained in patients after weight reduction by fasting (7) we believe that at least the elevation in HDL is caused by

the weight loss as such and not by caloric restriction.

There seems to be a general agreement that the LPL activity in adipose tissue in obese patients, expressed per cell, is increased in obese subjects, whereas the enzyme activity, expressed per gram tissue, is normal (14). In the present study on morbidly obese patients, the cellular LPL activity was not clearly elevated and the mean enzyme activity in postheparin plasma was below the reference range. Possibly, the comparatively low enzyme activities among our patients may be related to a minor weight reduction (on the average 1,5 kg) occurring prior to surgery. These findings do not support the view that increased LPL activity in adipose tissue plays a primary role for the development of obesity (35).

Our results on postheparin plasma LPL activities, which were slightly lowered after surgery, also indicate that the decrease in plasma TG levels was due to a decrease in VLDL production rate rather than to an increase in TG removal. The rise in Intralipid removal rate, therefore, must be interpreted as a consequence of the lowered plasma TG levels rather than as an indication of accelerated TG elimination; it is well known that the IVFTT is greatly influenced by the plasma TG pool size (33).

Hepatic lipase activities decreased significantly after weight reduction, which may be due to the decrease in plasma insulin levels (37).

In the present investigation we could not demonstrate the relationships between LPL activities and plasma triglyceride levels and HDL cholesterol concentrations, which might be expected from current views of lipoprotein metabolism (38). We believe that, in this particular situation, an influence of LPL on plasma triglyceride levels is masked by more marked changes in triglyceride secretion from the liver. Similarly, the effect of LPL on plasma HDL levels seems to be overridden by the significant changes in HL activity. The simultaneous decrease in HL activity and rise

in HDL cholesterol levels supports the view of HL as an enzyme involved in the degradation of HDL components (38).

In summary, our study confirms the frequency of abnormalities in lipid and carbohydrate metabolism in an obese population. A marked improvement in glucose and lipid metabolism was found and remained for at least 18 months after gastroplasty. Weight reduction/loss in body fat as such, rather than lowered caloric intake, seems to be important for the favourable metabolic changes registered. Our findings strongly support the view that risk factors of coronary heart disease and development of diabetes are greatly improved by gastroplasty in morbidly obese patients, partly by the weight reduction as such and partly by the improved metabolic pattern.

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ADIPOCYTE HEAT PRODUCTION BEFORE AND AFTER WEIGHT REDUCTION BY GASTROPLASTY

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Key words: obesity, microcalorimetry, thermogenesis, gastroplasty, thyroid hormones, insulin resistance, isolated fat cells, lipoprotein lipase.

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ABSTRACT

Fifteen grossly obese patients were studied before and 6-8 months after gastroplasty. Their mean body weight decreased by 30 % (from 127 ± 13 to 97 ± 14 kg, mean $\pm$ SD). The preoperative hyperinsulinemia, hyperglucosemia and hyperglucagonemia were significantly reduced at follow up. Lipoprotein lipase activity, measured in post-heparin plasma, was slightly reduced and did not change after weight reduction. Variables reflecting thyroid function were within the reference ranges; small but statistically significant reductions in serum thyroxine and reverse triiodothyronine levels were recorded. Adipocyte heat production, reflecting total cellular metabolic activity and registered by microcalorimetry, was significantly decreased before surgery (by about 60 % when expressed per g tissue and by about 20 % when expressed per cell) and increased significantly at follow-up; expressed per cell, the heat production was normalized, but expressed per g tissue the value were still about 15 % below those of a control group. The rise in heat production tended to be correlated to the decrease in body weight ($0,1 > p > 0,05$). The results indicate that the reduced adipocyte heat production in obese individuals is a consequence rather than a cause of severe obesity.

INTRODUCTION

Obesity is associated with profound alterations in glucose and lipid metabolism (1,15,17,18,19). Most of these changes represent an adaptation to overweight or to metabolic disturbances following the obese state, rather than causes of obesity. It is also well documented that adipocyte metabolism is greatly abnormal in obese individuals (2,3,10,19,26). We have recently shown that the total metabolic activity of adipocytes can be quantitatively and sensitively measured by microcalorimetry (9). Adipocytes from obese individuals had a significantly lower metabolic activity compared to those from lean individuals (23). After a moderate (15 %) weight reduction heat production from adipocytes increased, but the values were still lower than those obtained from lean subjects (23). It is not yet clear, whether the reduced adipocyte heat production is a primary factor contributing to the development of obesity or a phenomenon secondary to the obese state. Therefore, we have evaluated the effects of a rapid and significant (30 %) weight reduction on heat production from adipocytes in subjects examined before and 6 months after gastroplasty surgery for morbid obesity.

In the present study we have also related heat production values measured by microcalorimetry to adipocyte cell size and variables reflecting glucose and lipid metabolism and thyroid function, which may be of importance for the metabolic activity and cellular heat production.

MATERIAL AND METHODS

Patients and experimental design

Fifteen patients, 12 women and 3 men, between the ages of 23 and 41, participated in the study (Table I). They all had a long history of

overweight and were selected for the study because of severe obesity. High age (above 50), history of cardiovascular disease, diabetes demanding insulin treatment, and previous psychiatric disorder as well as known alcoholism, were considered contraindications for surgery. Three patients had chemical diabetes, as defined by fasting glucose levels above 7 mmol/l. Except for the typical metabolic concomitants of obesity, no patients showed signs of endocrine disease. The patients were operated by the same operating team. Essentially the operative technique described by Gomez (7,14) was used. The patients were encouraged to reduce weight before surgery and the mean weight loss prior to surgery was 1,5 kg. The investigations were performed under standardized conditions in the ward before surgery and 6 - 8 months after surgery. The initial body weight at operation ranged from 112 to 158 kg; the body weight after 6 and 12 months was 82 - 135 kg and 75 - 135 kg, respectively (Table I). Mean body weight 12 months after surgery was 93,6 kg ($\pm 17,4$ kg).

Twelve apparently healthy individuals, matched for sex and age served as a control group with regard to the microcalorimetric measurements. None of them had registered any significant weight change during the 2 months preceeding the study.

Blood and tissue samples were taken in the morning after the subjects had been fasting for 10 -12 hours.

Adipocytes

After local anesthesia with 1 % Carbocain^R open surgical biopsies were taken in the gluteal region. The biopsy material was cut in pieces and incubated for 30 min at 37°C in Krebs-Ringer-bicarbonate (KRB) buffer (pH 7,4) containing collagenase (3,3 g/l), albumin (30 g/l), insulin (0,1 U/ml) and glucose (11 mmol/l) while shaking at 180 cycles/min (10). The fact that no floating fat was observed in the adipocyte suspensions

indicated that there was no significant cell breakage during the preparation procedure. The suspensions were then filtered through gauze and the adipocytes washed with KRB-buffer containing the same amounts of insulin and glucose as during the incubation procedure. The suspension used for the microcalorimetric measurements contained 50 % (v/v) cells, in a KRB-buffer with insulin (0,1 U/ml) and glucose (11 mmol/l). Adipocyte size was measured by light microscopy. One hundred cells were measured and from the mean cell diameter the mean cell volume and triglyceride content were calculated.

Microcalorimetry

Microcalorimetry was performed as described earlier (9). The ampoules were charged with 0,9 ml cell suspension. Two microcalorimeters of the thermopile heat conduction type were used (22,24). After the calorimetric measurement the cell suspension was quantitatively washed out of the calorimetric ampoule with isopropanol. After partition against an acidified aqueous phase, the isopropanol was evaporated under nitrogen. The number of cells could then be calculated from the lipid weight of the isopropanol extract and the mean triglyceride content per cell.

Other methods

Lipoprotein lipase (LPL) activity was determined in postheparin plasma drawn 10 min after the injection of 50 U-heparin/kg body weight (11). One mU of enzyme activity represents the release of 1 nmol fatty acid per minute. Thyroxine was measured with a competitive binding protein technique (20), the T3 resin uptake test was performed according to Nosselin (13) and insulin, glucagon and triiodothyronine were measured by radioimmunoassay (4,8). Free T4 (FT4) was calculated using the methods described by Robbins (16). Total body ^{40}K was determined by a whole body scanner

calibrated with a phantom. Lean body mass and body fat were estimated according to Forbes (6).

Wilcoxon's rank order test was used for statistical evaluations of differences. Correlations between variables were calculated using Spearman's rank correlation test. The experimental data have been compared to the reference ranges routinely used at the laboratory or, when indicated, to a control group of 12 normal weight individuals matched for age and sex.

RESULTS

The mean body weight reduction 6 months after surgery was 30 kg (range 18 - 42 kg); about 70 % could be accounted for by reduction in body fat (Table I). Fat cell volume decreased by 33 % (Table I).

Table I. Morphometric data of 15 patients before gastroplasty and at follow-up 6-8 months postoperatively. Data are given as mean $\pm$ SD.

	Before	After
Body weight (kg)	127 $\pm$ 13	97 $\pm$ 14
Body fat (kg)	73 $\pm$ 13	52 $\pm$ 8
Lean body mass (kg)	54 $\pm$ 9	45 $\pm$ 9
*) Fat cell size (μ g lipid/cell)	0.639 $\pm$ 0.13	0.430 $\pm$ 0.08

*) Reference values 0.24-0.52 μ g lipid per cell.

Before weight reduction mean fasting blood glucose levels and mean plasma insulin concentrations were elevated, indicating insulin resistance (Fig 1). Weight reduction was associated with a decrease in mean basal insulin levels of more than 50 % ($p \leq 0,025$) and almost a 30 % reduction in mean fasting blood glucose concentration (Fig 1) which was highly significant ($p \leq 0,005$). Similarly, the elevated plasma glucagon levels decreased significantly ($p \leq 0,025$).

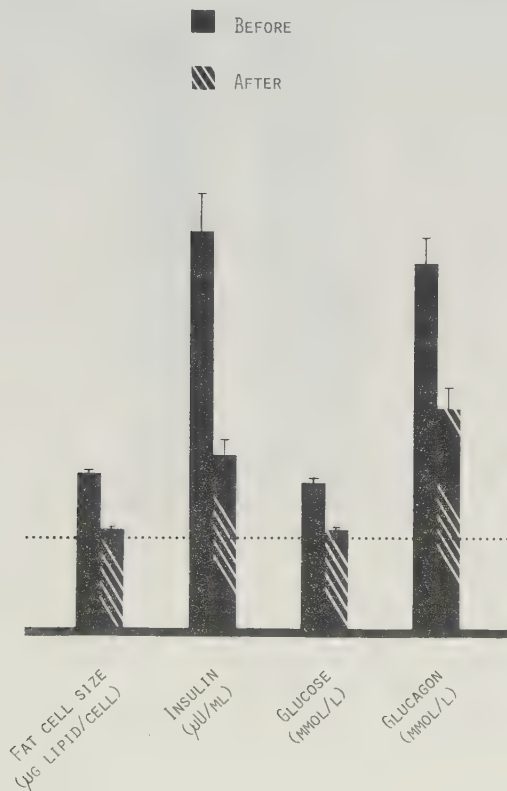


Figure 1 Fat cell size and variables reflecting glucose metabolism in 15 obese patients before and after weight reduction by gastroplasty. Data are given as mean $\pm$ SEM. The dotted line indicates modal class, i.e. for glucose 4.0 mmol/l, insulin 5.0 μ U/ml and glucagon 50 μ g/ml.

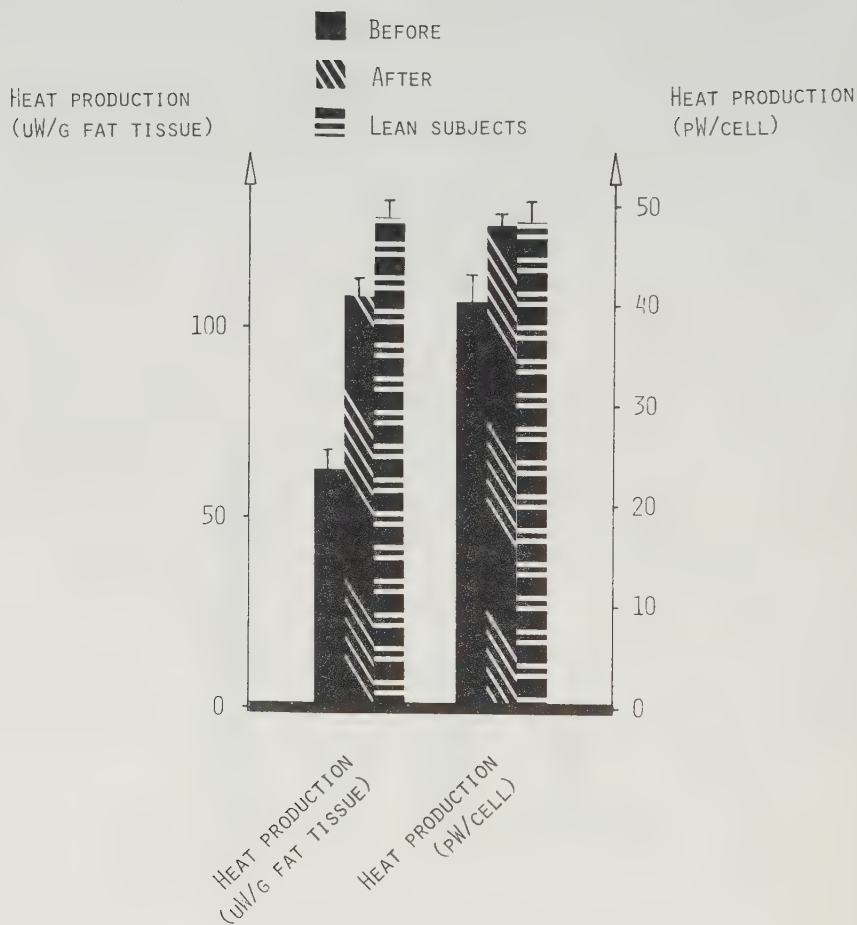


Figure 2 Adipocyte heat production in lean subjects and in obese patients before and after weight reduction by gastroplasty. Data are given as mean $\pm$ SEM.

Thyroid hormon concentrations were within the normal range before and after treatment. The decrease in S-T₄ and S-rT₃ after surgery was about 10 % ($p \leq 0,05$) (Table II). A moderate change in S-TBPm and TBPA was also found statistically significant (Table II), whereas S-TBG, S-I₃ and S-TSH remained unchanged after treatment.

The mean activity of LPL in postheparin plasma before surgery was $62 \pm 5,0$ mU/ml, which was slightly below the reference values (70 - 145mU/ml) and decreased slightly postoperatively although the decrease did not reach statistical significance.

The heat production per cell and per g fat tissue was significantly lower before surgery in our obese patients than in lean subjects (Fig 2). After weight reduction, heat production in adipocytes increased by 72 % ($p \leq 0,001$), when expressed per g fat tissue, but only by 17 % (n.s.) when expressed per cell.

Table II. Variables reflecting thyroid function before gastroplasty and at follow-up 6-8 months after surgery . Data are given as mean $\pm$ SD. ns, non significant.

	Reference values	Before	After	
S-T ₃ (nmol/l)	1.5-3.0	2.2 $\pm$ 0.4	2.2 $\pm$ 0.4	ns
S-T ₄ (nmol/l)	51-154	128 $\pm$ 20	117 $\pm$ 18	$p \leq 0,05$
S-rT ₃ (nmol/l)	0.14-0.54	0.26 $\pm$ 0.6	0.23 $\pm$ 0.6	$p \leq 0,05$
S-TBPm (arb U)	0.8-1.2	0.95 $\pm$ 0.13	0.88 $\pm$ 0.13	$p \leq 0,05$
S-TSH (U/l)	0-8	3.13 $\pm$ 1.36	3.0 $\pm$ 0.85	ns
S-TBPA (μ g/ml)	180-300	242 $\pm$ 38	202 $\pm$ 57	$p \leq 0.005$
S-TBG (μ g/ml)	12-24	20.55	20.56	ns
S-FT ₄ (nmol/l)	16-30	30.7 $\pm$ 3.9	29.6 $\pm$ 5.3	ns

Correlations

Cell size before treatment was significantly correlated to total body fat ($p \leq 0,025$) and the decrease in cell size after weight reduction was significantly correlated to the decrease in total body fat ($p \leq 0,025$).

Analysis of the relations between heat production values and morfometric data demonstrated that the increase in heat production (Fig 2) tended to correlate to the decrease in body weight ($p \leq 0,1$).

Thyroid hormone concentrations and heat production values yielded the following correlations: before surgery, FT4 and adipocyte heat production tended to correlate ($p \leq 0,1$), and the decrease in FT4 was significantly ($p \leq 0,05$) correlated to the rise in heat production after treatment. Also, the increase in heat production was negatively correlated ($p \leq 0,02$) to the decrease in S-rT3, i.e. the heat production tended to rise more in the patients, who had the smallest decrease in S-rT3.

There were trends indicating that plasma insulin concentrations after surgery were correlated to postoperative heat production (although not statistically significant), and a similar correlation trend was also found between differences in pre- and postoperative heat production and differences in plasma insulin concentrations. These trend did not reach statistical significance, probably because the preoperative p-insulin values ranged considerably (Fig 1).

Changes in other variables reflecting thyroid function or glucose metabolism were not significantly related to the change in adipocyte heat production.

The weight reduction registered was negatively correlated to the decrease in FT_4 ($p \leq 0,05$), that is patients who lost most weight showed the smallest decrease in FT_4 values, and the same trend was found regarding $S-rI_3$

DISCUSSION

Abnormalities in adipose tissue metabolism in obese individuals, such as increased LPL activity (5,21), decreased sensitivity to insulin (1,19) and increased lipolysis (2), have been well documented. All biochemical reactions in a cell lead to the dissipation of heat and in the present study we have employed microcalorimetry, which allows quantitative measurements of total metabolic activity, to further characterize the disturbed adipocyte metabolism in obese subjects.

Our data reflecting glucose metabolism confirm the general metabolic pattern found among obese individuals. After weight reduction the preoperative hyperinsulinemia and fasting hyperglycemia decreased significantly, indicating a reduction of peripheral insulin resistance. The changes in these variables strongly support the general view that these derangements reflect alterations secondary to the obese state.

Our data on LPL activity in postheparin plasma before and after weight reduction do not support the view, that alterations in LPL activity may represent an early and possibly primary defect in the development of obesity (21). The comparatively low enzyme activities among our patients may be related to a minor weight reduction (on the average 1,5 kg) occurring prior to surgery.

All variables reflecting thyroid function were within the normal range before and after weight reduction and changed little, although the moderate reductions in $S-T_4$, $S-rT_3$ and $S-TBPm$ were found to be signifi-

cant (Table II).

In this study microcalorimetric measurements were performed in the presence of glucose and insulin in order to maximally stimulate major metabolic pathways within the adipocyte. Before weight reduction heat production was significantly lower than in lean individuals, whether expressed per g fat tissue ($p \leq 0,005$) or per cell ($p \leq 0,05$). After weight reduction heat production increased significantly when expressed per g fat tissue ($p \leq 0,001$), but expressed per cell this increase in heat production did not reach statistical significance. However, as could be expected cell size decreased (by 33 %) due to the reduction in body fat and after weight loss cell size was in the upper part of the normal range, although the patients were still overweight (Table I). Thus, the patient's obesity after surgery in general could be classified as hyperplastic. After surgery and weight loss, heat production, when expressed per cell, did not differ from the heat production found in lean subjects (Fig 2).

In an earlier report (23), we have found significant correlations between heat production and plasma insulin levels after a moderate weight reduction and the same trends could be confirmed in this study, where the caloric intake was considerably lower (around 1000 kcal/day) than in our previous investigation (23) (1700 kcal/day); a fact which may have influenced our data. We could also register significant correlations between alterations in different variables reflecting thyroid function and changes in heat production from adipocytes. These correlations were not found in our earlier investigation (23), probably because weight reduction and the alterations in thyroid function were less marked. The results of the present study, however, are consistent with our recent finding that hypothyroid patients have a clearly lowered heat production, which normalizes upon treatment (25).

Even if a small deficit in energy expenditure over a long period of time may lead to the development of obesity, our data from this investigation

indicate, that the decreased heat production found in adipocytes from obese individuals, as many other metabolic alterations, is a secondary phenomenon to the obese state rather than a primary pathogenetic factor. Especially, when comparing data on adipocyte heat production from different groups of patients, including lean subjects (Fig 3), the relation between body weight and heat production makes it tempting to conclude, that the lowered heat production represents a consequence rather than a cause of obesity. However, these data are mean values, a fact, which may make generalizations hazardous. Potentially, however, the reduced cellular heat production in obese subjects represents a factor, which may tend to perpetuate the obese state.

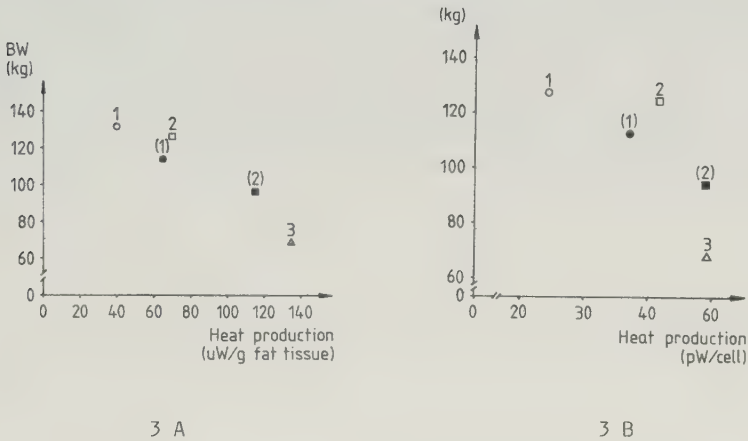


Figure 3 Adipocyte heat production in lean subjects (3) and in obese patients before (O □) and after (● ■) weight reduction by fasting (1) and gastroplasty (2). Results from the group treated by fasting (1) are from ref. 21. Data are expressed per g adipose tissue (3A) and per cell (3B).

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WEIGHT LOSS AFTER GASTROPLASTY: PSYCHOLOGICAL SEQUELAE IN RELATION TO
CLINICAL AND METABOLIC OBSERVATIONS.

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KEY WORDS: Obesity; gastroplasty; weight reduction; psychological testing.

surgery compared to responders (Leon et al 1979), the argument that "it seems unlikely that the patients with negative reactions would be unwilling to respond or report them" (Harris and Green 1982), is hardly tenable. Unfortunately in many reports (e.g. Gomez 1981) the number of patients reported in follow-ups differ considerably from the original patient sample. As concluded by Andersen et al (1980), due to methodological weaknesses in evaluation, recommendations of bariatric surgery, positive or negative, seem to reflect the authors' attitude rather than objective data.

The present study, as an alternative to describing average postoperative effects which tends to contaminate the issues of patient selection and operational sequelae, investigates subgroups of patients showing a more or less successful weight reduction 18 months after gastroplasty. While many reports have been published on the surgical aspects of gastroplasty (Gomez 1981; Freemant and Burchett 1980), we have located no previous study which deals with psychological aspects of this treatment. Over 90 % of total weight loss after gastroplasty occurs in the first year after surgery and no long-term follow-ups have been reported. Thus, our study deals mainly with the psychological sequelae in relation to clinical and metabolic observations following the initial adaptation to this treatment.

MATERIAL AND METHODS

Patients

Twenty-one patients, 17 women and 4 men, between the ages of 23 and 44, were included in the study. Sixteen patients had a history of overweight since childhood and all had a history of intractable obesity and documentation of trial at weight reduction with conservative treatment. The additional five patients all developed their obesity during and after their first pregnancy. Several patients claimed to suffer from depression due to their overweight, although

only one had been treated with antidepressive drugs. In the history of three patients we found an alcohol consumption above average.

At operation the mean body weight in our material was 126 kg (93-192) and the mean Broca's index^{*} was 2.0 (1.6-3.2). Before surgery the patients were encouraged to reduce weight and our lightest patients managed to reduce her weight from 110 to 93 kg. Our heaviest patient reduced his weight from 220 to 190 kg.

At or before admission to the hospital all aspects of the surgical procedure, including mortality and morbidity, were discussed with the patients and they also underwent extensive metabolic, gastrointestinal, pulmonary and psychological investigations.

Operative technique

All patients were operated upon 1979-1980 by the same operating team. A slight modification of the operative technique described by Gomez (1981) was used (Olsson et al 1983). Postoperatively Cimetidine was used during less than one week and after that no drugs, except vitamins, were given.

Follow-up

At the time of this study all patients had been followed at least 18 months after the operation. The routine postoperative follow-up included a monthly visit for the first three months and a visit every three months thereafter. A complete postoperative clinical and metabolic investigation was performed 6-8 months after the operation.

$$* \text{ Broca's index} = \frac{\text{weight (kg)}}{\text{length (cm)} - 100}$$

RESULTS

Weight loss

The average weight loss for the entire group six months after surgery was 29 kg. Eighteen months postoperatively we found a mean weight loss of 30.4 kg (range 1-72 kg). The patients were divided into three groups (Fig 1), A, B, and C which showed constant differences in weight loss after surgery as confirmed by a significant time $\times$ groups interaction in a two-way ANOVA. Rank correlations computed on the entire groups for weight at 6 and 12 months and 6 and 18 months, respectively, were highly significant ($r_s = .89$ and $.89$; $p < 0.001$), providing further evidence that weight changes followed consistent patterns which were already established six months after surgery. The patients in the C group constitute 35 % of the samples, a failure rate, which was also found by Freeman and Burchett (1980).

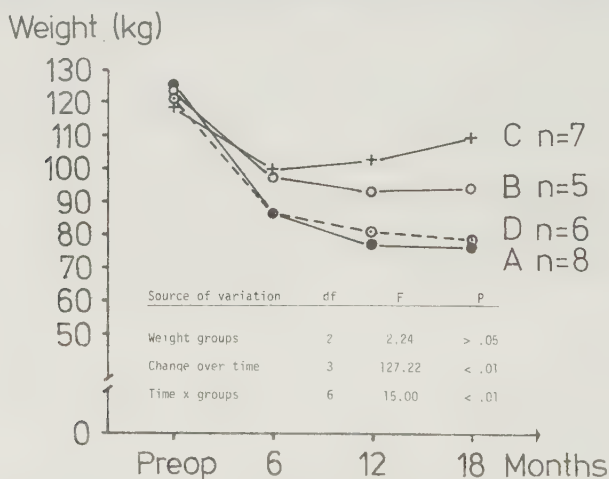


Fig 1

Differential developments of weight loss after gastropasty in three groups of patients (A-C). Additionally, the weight loss of the six patients in the A and B groups scored for depression (group D) postoperatively is shown with a dotted line. One patient, classified in the B group because of his pattern of weight loss (192, 163, 157 and 157 kg, respectively) has been excluded from this figure on account of his exceptional size.

The six patients, all from the A and B groups, which were scored for depression (group D in Fig 1) in the postoperative MCT test (see below) showed the same pattern of weight loss as the patients in group A.

Early and late surgical complications in relation to weight loss and postoperative depression

Two patients classified into groups B and C, respectively, had to be reoperated and drained because of leakage from the upper pouch. They both had uneventful postoperative courses after the reoperation. One patient in group B developed a deep iliac vein thrombosis which was successfully removed.

Prolonged vomiting occurred in two patients classified into groups A and C, respectively, which required short re-admission to the hospital for intravenous fluids due to electrolyte disturbances. In addition, two patients in group A and one patient in group C complained of severe vomiting, especially when eating certain types of food, but their problems could be solved without rehospitalization.

The frequency of verified staple line rupture, average position in operation series, and dilation of the channel or dilation of the upper gastric pouch in the three different groups are shown in Table I. Most of the staple line ruptures and dilations of the channel were discovered at the second check-up about 12 months after the operation and the patient could often tell at what time they had been able to eat without restrictions.

One out of the six cases scored for depression (see below) suffered from vomiting, although electrolyte disturbances was not noted. None of the other patients with early surgical complications showed signs of depression in the postoperative tests. The late postoperative complications, i.e. staple line rupture, dilation of the pouch or the

channel was mainly found in the C group, where few signs of depression could be found (Table IV).

As seen in Table I average position in the operation series - a factor which may influence the outcome of the operation and the postoperative psychological tests - did not differ between the groups.

Table I

Distribution of late postoperative complications and average position in operation series in group A, B, C and D (see text).

	A (n=8)	B (n=6)	C (n=7)	D (n=6)
Average position in operation series	11.3	9.0	10.4	10.0
Enlarged channel	2	2 (+1?)	7	1
Enlarged pouch	2	1	-	2

Metabolic observations following weight loss

Body weight and the different biochemical variables analysed in the groups A + B (judged as successful cases), C and D before and at follow-up 6-8 months after surgery are shown in Table II.

Variables reflecting thyroid function decreased considerably in groups A + B and D, whereas the same parameters in the C group, with least weight reduction, remained unchanged at the follow-up 6-8 months after surgery.

Similarly, measurements reflecting glucose metabolism showed differential changes between the groups. The decrease in plasma insulin and plasma glucagon was most prominent in the groups with the greatest weight loss.

Table II

Biochemical variables in groups A+B, C and D (see text) before gastropasty(I) and at follow up 6-8 months postoperatively(II). Data are given as mean $\pm$ s.e.m.

	A + B		C		D	
	I	II	I	II	I	II
s-T ₃ (mmol/l)	2.07 $\pm$ 0.12	1.76 $\pm$ 0.14	2.10 $\pm$ 0.16	2.22 $\pm$ 0.09	2.26 $\pm$ 0.22	1.65 $\pm$ 0.18
s-T ₄ (mmol/l)	146 $\pm$ 6.55	119 $\pm$ 5.80 ^{a)}	136 $\pm$ 16.7	149 $\pm$ 17.3	158 $\pm$ 9.17	100 $\pm$ 9.12
s-rT ₃ (mmol/l)	0.267 $\pm$ 0.017	0.248 $\pm$ 0.025	0.270 $\pm$ 0.034	0.210 $\pm$ 0.023	0.280 $\pm$ 0.032	0.220 $\pm$ 0.019
p-insulin (mmol/l)	18 $\pm$ 5.7	6.7 $\pm$ 1.3	21 $\pm$ 5.5	11 $\pm$ 4.8	22.2 $\pm$ 9.9	5.3 $\pm$ 1.48
p-glucagon (mmol/l)	141 $\pm$ 36	102 $\pm$ 27	231 $\pm$ 21	191 $\pm$ 21	199 $\pm$ 48	111 $\pm$ 42
s-cobalamine (pmol/l)	369 $\pm$ 30	227 $\pm$ 17 ^{b)}	377 $\pm$ 55	320 $\pm$ 52	455 $\pm$ 44	314 $\pm$ 88
b-folate (mmol/l)	122 $\pm$ 11	73 $\pm$ 11 ^{b)}	168 $\pm$ 21	86 $\pm$ 12	126 $\pm$ 22	54 $\pm$ 9
s-uric acid (umol/l)	416 $\pm$ 17	394 $\pm$ 30	402 $\pm$ 39	334 $\pm$ 43	414 $\pm$ 30	307 $\pm$ 49
Body weight (kg) $\pm$ SD	125 $\pm$ 12	91 $\pm$ 12	119 $\pm$ 19	99 $\pm$ 18	119 $\pm$ 16	86 $\pm$ 15

a) $p \leq 0.05$ compared to preoperative values

b) $p \leq 0.005$ compared to preoperative values

Postoperatively, S-cobalamins and B-folate values also decreased considerably, even in C group, although no patient developed an anaemia during the follow-up period. The serum levels of uric acid also showed a considerable decrease in all groups after surgery.

Fat cell size determined before surgery did not differ between the groups and serum endorfine concentrations exceeding 10 pg/ml were not found in any of our patients.

Psychological sequelae following weight loss

MCT test. Fourteen patients were MCT-tested before and 18 patients after surgery; 12 patients participated on both occasions. A comparison of the pre- and postoperative MCT-protocols from these 12 patients reveals two main changes. First, taken together, signs of regressive defence and signs of immature and/or inadequate identity have decreased considerably. Second, eight patients are scored for depression after surgery as compared to none before surgery (Table III).

Table III

Distribution of signs per person of regressive defence + immature and/or inadequate identity, and depression, in MCT in 12 patients tested both before and after surgery. + denotes presence and - absence of sign.

	Regressive def + imm and/or inadequate id		Depression	
	+	-	+	-
MCT before surgery	12	0	0	12
MCT after surgery	7	5	8	4

$p \leq .05$

$p < .01$

Fischer's exact test, two-tailed

The same pattern is obtained when all the available MCT-protocols are compared. Signs of regressive defence decreased from 86 % to 44 % (12/14 vs 8/18) and signs of depression increased from 7 % to 61 % (1/14 vs 11/18). The large increase of signs of depression after surgery refers to stereotyped repetitions of reports which clinically correlate with mild to moderate symptoms of depressive retardation (Eberhard et al 1965). Out of the 11 patients who were scored for

depression after surgery of which nine belonged to the A and B groups. A further comparison of the weight groups was made by applying a more restrictive scoring of stereotyped repetition to differentiate more and less pronounced cases of depressive retardation. The more restricted scoring yielded six cases of depression, all patients within the A and B groups. A comparison of only those 12 patients, where both pre- and postoperative protocols are available, yields similar results. Eight patients show signs of depression after surgery; six of these belong to the A and B groups. When a restrictive scoring is applied three patients still remain, all in the A and B groups. Thus, it seems possible that more marked depressive reactions are more prevalent in those patients who have lost the most weight. This inference is substantiated by the additional observation that out of four patients who developed acute depressive reactions three belonged to groups A and B.

Table IV

The distribution of signs per person in MCT in the three weight groups A, B and C after surgery.

Signs or combination of signs in MCT	A (n=8)	Weight group B (n=6)	C (n=4)
a. all combinations with repression, isolation and projection	6	4	1
b. depression + anxiety (2) or sensitivity (1)	1	2	0
c. C-phase without previous defence or denial	1	0	3
	A + B	C	
a + b	13	1	
c	1	3	

p = 0.001 (Fisher's exact test)

An analysis of the 18 MCT-protocols obtained after surgery (Table IV), yielded a higher proportion of repression, isolation and projection

or, alternatively, mainly signs of depression in groups A and B compared to group C. Group C, on the other hand, included, with one exception, the only signs of denial and C-phase without previous defence. Thus, the patients who did poorly employed an immature defence (Smith and Danielsson 1982), or had no effective defence to avert anxiety.

Clinical postoperative ratings. Four patients, two from group A and one each from groups B and C, developed depressive reactions severe enough to need professional intervention. As already noted this difference between the groups may be compared with the higher incidence of more severe signs of depressive retardation in the MCT-test in groups A and B compared to group C.

All patients in the C group were disappointed with the operation and tended to put the responsibility for their failures on factors outside their own control, whereas 12 out of 13 patients in the A and B groups were satisfied.

Non-significant trends were found indicating that the patients in the C group and the depressed patients in the A and B groups more often had a childhood onset of obesity. These trends agree with earlier findings (Stunchard and Rush 1974), that patients with childhood onset of obesity are more vulnerable than are those with adult onset of obesity.

DISCUSSION

In many patients the gastric partitioning techniques for morbid obesity lead to a significant reduction of body weight. In the preoperative opinion of these patients, weight reduction would strongly improve their psychological state. Nevertheless many patients have psychological problems following weight reduction after surgical intervention. Many of these problems could, at least theoretically, be

attributed to early or late surgical complications or metabolic disturbances following the surgical procedure. However, no correlations at all could be found between early and late surgical complications or metabolic disturbances after gastroplasty and postoperative depression implying that these factors do not primarily influence the patients' postoperative psychological status.

In general the metabolic response to weight reduction in this study is consistent with earlier results from studies on fasting therapy (Sörbris 1981; Sörbris et al 1982). However, it is evident that the changes in some variables, e.g. thyroid hormones and possibly insulin and glucagon were more marked in the patients with the greatest weight loss. The patterns registered in groups A + B and group D were strikingly similar although with a limited number of subjects differences compared to group C did not reach statistical significance. All the patients had plasma β -END concentrations within the normal range (10-30 pg/ml) before and after treatment. These data demonstrate that basal β -END concentrations are not affected by loss in body weight.

An evaluation of differences in psychological test results obtained before and after surgery has to consider that the preoperative investigation was made only a few days before surgery and may have been affected by preoperative stress. As shown by Janis (1957), a major operation constitutes a threat to the patient's physical and mental integrity. The overall decrease in signs of immature and/or inadequate identity and regressive defenses in the postoperative MCT test support this argument and indicate that the preoperative results do not reflect the patient's habitual mode of functioning. However, signs of immature defenses were found in the postoperative protocols as well, particularly in the C group (Table IV), an observation suggesting that these patients' immature defensive organization is a characteristic, habitual feature.

An additional effect of preoperative stress may have been that habitual mild or moderate depressive tendencies were temporarily concealed and replaced by alternative strategies to avert anxiety (cf. Rydén and Danielsson 1983). To control for the effects of preoperative stress on the MCT results, a comparison was made with MCT protocols obtained from a sample of 20 obese patients of similar age and weights investigated in a follow-up study on average two years after a fast treatment (unpublished data. Four (1/5) of these patients had been scored for depression as compared to 2/3 of the surgical patients ($\chi^2_C = 6.83$, $p < 0.1$). Thus depressive reactions seem to be concomitant to weight reduction after gastroplasty. This finding agrees with the results of several previous studies of patients on standard medical treatment for obesity, 50 % of whom tend to experience untoward emotional reactions, particularly anxiety and depression, a percentage which may increase to 100 in morbidly obese patients (Stunchard and Rush 1974; cf Halmi et al 1980). Thus, in the present sample objective evidence show that dysphoric reactions were not limited to specific clear-cut cases of clinical depression but to a varying extent affected approximately two thirds of the patients of which four (19 %) developed acute depressive reactions.

This finding is inconsistent with many reports based on questionnaire data but is consonant with evidence obtained in studies where the postoperative adaptation has been followed closely (Castelnuovo-Tedesco 1980; Espmark 1979). Selfratings and questionnaires may produce misleading data, as many patients with psychological problems tend to be underrepresented in follow-ups (Leon et al 1979) (refuse to answer) and others, pleased with the many positive effects related to their weight loss, may tend to de-emphasize or deny any negative effects noticed.

On a common sense basis, it may be expected that the patients who did not loose weight satisfactorily would experience more severe psychological problems. The opposite outcome found here indicates that a rapid

and substantial weight loss and/or the enforced reduction of food intake involve problems of adaptation. Previous reports indicate that two interrelated processes contribute to such problems. During weight loss many patients gain an enhanced self-esteem and an increased self-assertiveness which make them feel less obliged to please those around them. Not seldom, reactions from spouse and friends are ambivalent or outright negative (Title 1973) and the patient, being unaccustomed to act independently, gets feelings of guilt and subsequently become anxious and/or depressed (Solow et al 1974; Castelnovo-Tedesco 1980; Espmark 1979). Consequently, Weisz and Bucher (1980) found that an active participation of the spouse in therapy may ease depression during weight loss. Grossly obese individuals have often developed passive-dependent or passive-aggressive traits. These personality features may be consequences of the obese condition (Rhodin 1981) or be adaptations to an early developed insecure sense of separate identity (Bruch 1973). The latter explanation is consonant with the psychological test results in this study, in particular the preoperative MCT scores which yielded signs of immature sense of self for half of the patients (Rydén and Danielsson 1983). Separation from narcissistic supplies, such as food and nurturing relationships, in such individuals, tend to induce depressive reactions as a defense against anxiety (Sandler and Joffe 1965; Wohlman 1981).

In conclusion, a majority of our patients who showed a satisfactory postoperative weight loss, developed depressive reactions which in most cases were mild to moderate. Further, the more successful patients had more mature defenses. We have shown earlier (Olsson et al 1983) that the successful patients appraised the operation more realistically in a preoperative interview; they also lived in a more supportive social situation. The patients who lost the most weight (group A), also were the most field-dependent, implying an inclination to rely on those around them, particularly in ambiguous situations (Witkin and Goodenough 1981). Postoperative adaptation thus seems to

be promoted by an adequate defensive organization, a realistic attitude and a supportive family, the latter being particularly important for field-dependent individuals.

The less successful outcome for the patients in the C group seems to derive from two factors in particular, one being a reluctance, of which they are not quite aware, to be put through an enforced process of growing up. Secondly, once operated they are liable to perceive and react with anxiety to even minor somatic side effects and to be less able to tolerate the necessary food restriction. Further, they can be expected to put the responsibility for the outcome of surgery, or any therapy, on factors outside their own control.

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WEIGHT REDUCTION AFTER GASTROPLASTY - THE PREDICTIVE VALUE OF SURGICAL,
METABOLIC, AND PSYCHOLOGICAL VARIABLES

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ABSTRACT

Twenty-one grossly obese patients (mean body weight 126 kg, range 93-190 kg) were treated with gastroplasty ad modum Gomez. Eighteen months after surgery the average weight loss was 30.4 kg (range 1-71 kg); about 80 % of this weight loss represented loss of body fat. Mean weight loss of the entire programme, including preoperative weight reduction, was 34.4 kg (range 1-71 kg). Dilation of the pouch and/or channel occurred in 14 patients and was generally discovered 6-12 months after operation.

The wide range in weight reduction could not be unequivocally attributed to technical - surgical factors. Although the patients with the least weight reduction had all developed channel dilation, several patients with excellent weight loss also showed dilation of the pouch and/or channel. An extensive psychological investigation performed before surgery demonstrated more signs of sensitivity and denial in the unsuccessful patients; the successful ones were more dependent and tended to live in a supportive social environment. The unsuccessful patients were younger and their estimated alcohol consumption was higher. A number of morphological and biochemical variables including body weight, fat cell size, and variables reflecting thyroid function, lipid and glucose metabolism, and adipose tissue metabolism, were not related to subsequent weight loss.

INTRODUCTION

With conservative treatment, few morbidly obese patients attain satisfactory, long-term weight reduction (4, 27). In contrast, bariatric surgery is reported to achieve a success rate of approximately 85 per cent, defined as a loss of between 25 per cent and 50 per cent of excess weight (31). The development of gastric partitioning techniques, which have a lower rate of especially late postoperative complications than intestinal by-pass surgery, is increasing the attractiveness of surgical intervention as a treatment option (7). However, each sample of patients contain individuals who do not benefit from the treatment. Some patients are unable to follow dietary instructions during the postoperative period and show only insignificant weight loss at follow-up. Others develop crisis reactions which necessitate psychiatric treatment (5). There is conflicting evidence regarding the frequency and magnitude of these problems, no doubt as a consequence of differences in the specific methodologies used to assess outcome of treatment and also to differences between studies in the number of patients who fail to appear at follow-up. Leon et al (14) found a large proportion of non-responders at follow-ups with severe psychological and physical problems subsequent to surgery.

The question of how to identify unsuccessful patients preoperatively largely remains unsolved (3, 28); e.g. while running psychoses and alcoholism are considered as contraindications for surgery by most teams, there seems to be no agreement on more subtle criteria for selection of patients. With the exception of suggestions to exclude from surgery sedentary patients with low resting metabolic rates (27) or patients who are seriously ambivalent or have grossly unrealistic expectations (2), the roles of metabolic and psychological factors in determining outcome of surgery have not been established. Thus, apart from failures caused by surgical complications per se, it remains unclear why some patients do well and others poorly and therefore what can be done to identify "unsuccessful patients" before surgery.

The present study is based on a sample of 21 grossly obese patients who took part in extensive metabolic and psychological investigations before and repeatedly after gastroplasty. We report on inter-individual differences in weight reduction during a 18-month follow-up, as related to surgical factors and preoperatively assessed metabolic and psychological characteristics.

PATIENTS AND METHODS

Patients

The patients selected for the study came spontaneously to the surgical out-patient clinic or were referred there because of severe obesity. High age (above 50), history of cardiovascular disease, severe diabetes demanding insulin treatment and previous psychiatric disorder as well as known alcoholism, were considered contraindications for surgery.

Twenty-one consecutive patients, 17 women and four men, between the ages of 23 and 44, were included in this study. All had a history of intractable obesity for at least four years and documentation of attempts at weight reduction with conservative treatment. Several of the patients suffered pain from weight-bearing joints and most had social complications due to overweight. Three patients also had diabetes treated with sulphonylurea, and four had mild hypertension which required treatment (β -blockers and/or diuretics). None showed signs of severe metabolic or endocrine problems.

Before surgery patients were encouraged to loose weight. Our lightest patient managed to reduce her weight from 110 to 93 kg and our heaviest patient reduced his weight from 220 to 192 kg. The mean weight reduction before surgery was 4 kg (0-28 kg). At operation the mean body weight was 126 kg (93-192) and the mean Broca's index^{*)} was 2.0 (1.6-3.2).

*) Broca's index = $\frac{\text{body weight (kg)}}{\text{height (cm)} - 100}$

At or before admission to hospital all aspects of the metabolic studies and surgical procedure, including mortality and morbidity, were discussed with the patients. At admission they underwent extensive metabolic, gastrointestinal, pulmonary and psychological investigations.

Operative technique

All patients were operated upon 1979-1980 by the same team. The surgeons' general judgement of the surgical procedure was rated on a 5-point scale, the highest score being given when the operation had been difficult to perform (accidental splenectomy, severe adhesions etc). Operative technique was essentially that described by Gomez (7). In order to create the channel along the major curvature the C-clamp attachment for the TA-90 stapler was used; alternatively the five most distal staples were removed. Volume of the upper pouch was estimated by instilling saline solution through a nasogastric tube into the pouch which was closed proximally by a rubber band around the esophagus and distally by the TA-90 instrument. The volume was adjusted to 40-50 ml and staple rows applied. Most patients received only one application of the TA-90 instrument (16 out of 21) because of an unexplainable leakage from the upper pouch in one patient receiving two applications early in our series of operations. A large nasogastric tube (Charrières 30) was inserted and a sero-muscular suture, using 2-0 prolene, was applied around the tube to form a 11 mm channel. The large nasogastric tube was replaced by a smaller one to drain the proximal and distal parts of the stomach after the operation.

In a few cases abdominal drains were applied, but subcutaneous drainage was routinely used as well as antibiotic prophylaxis with doxycycline and antithrombotic prophylaxis with Macrodex. Ventilatory support was provided as indicated. Intensive care was not required.

Postoperatively Cimetidine was used during three days; thereafter the nasogastric tube was removed and the patient received a liquid diet followed by pureed diet after one week.

Metabolic investigations

Preoperative metabolic investigations were focused upon variables reflecting energy transport, adipose tissue metabolism and thyroid function. In order to minimize short-term effects of dietary composition and caloric intake on these measurements, patients were hospitalized for one week before surgery and given a balanced diet aimed at maintaining constant body weight. The sampling was not standardized in relation to menstrual cycle.

Body fat and lean body mass was calculated from determinations of endogenous ^{40}K , which was measured by a whole body gamma spectrometer calibrated by the use of a phantom. Lean body mass was then estimated by the formula described by Forbes (6). Body fat was calculated by subtracting lean body mass from the body weight.

Fat cell size was determined in surgical biopsy specimens obtained from gluteal fat. Adipocytes were isolated from the biopsy material by collagenase treatment (17). The fat cell suspension was washed by repeated centrifugation and fat cell size was measured on 100 cells from each sample under the light microscope. From the mean cellular diameter mean cell volume and triglyceride content were calculated.

The individual adipocyte heat production was determined by microcalorimetry (15). Lipoprotein and hepatic lipase activities in post-heparin plasma were measured by specific methods (16). Thyroxine (T_4) was measured with a competitive protein-binding technique (20); T_3 resin uptake test was performed according to Nosslin (18). Insulin, glucagon, triiodothyronine (T_3) and reverse triiodothyronine (rT_3) were measured by radioligand. Blood glucose was measured by the

glucose-oxidase method in samples obtained before and during an intravenous glucose load using 30 g/m^2 body surface. Cholesterol, triglycerid and HDL cholesterol were measured by enzymatic methods (24).

Psychological methods

The psychological investigation particularly stressed the patients' defensive organization, self-perception and cognitive characteristics. The detailed results of the preoperative psychological investigation have been published elsewhere (19). The present report deals primarily with data obtained with the Meta-Contrast Technique (MCT), the Rod-and-Frame Test (RFT), and a clinical interview.

MCT. The Meta-Contrast Technique is a process-oriented test within the field of personality description and clinical diagnostics with its theoretical framework being within the percept genetic theory (12, 23), which has its origin in experimental cognitive psychology and psychoanalytic theories. Its diagnostic efficiency has been demonstrated in numerous clinical studies (22). In the MCT two stimuli, A and B, are presented on a screen in front of the subject. Stimulus A (an ugly, forbidding face) implies a threat directed at the person depicted in B (a boy sitting at a table). The subject is first acquainted with B which is presented at gradually increasing exposure times until a correct description is given. Throughout the remaining test, B is presented at a standard exposure time which makes correct identification possible. Without the subject knowing it, A is then introduced immediately before B, first at brief exposure times, which are gradually prolonged. The presentation series is terminated when A is correctly reported by the subject. The test is scored on the basis of the subjects' verbal reports and, to some extent, non-verbal reactions. Attention is mainly focused on their way of handling the introduced threat in the previously established percept. Before correct recognition, A is often reported in a distorted fashion.

Perception of B may also change under the influence of the subliminal perception of A. Distortions and transformations of the A and B pictures are quite stable phenomena with forms known from the psychoanalytic theory of defense and correlating with clinical classification of psychopathological symptoms. In the present study, the following scoring dimensions were used: repression, isolation, projection, sensitivity, depression, denial, anxiety, and regressive defense. For a detailed description of the scoring categories see Rydén and Danielsson (19). A recent description of the MCT and its theoretical rationale is found in Smith and Danielsson (21).

RFT. The Rod-and-Frame Test yields measures of field-dependence-independence, a cognitive dimension reflecting psychological differentiation and related to interpersonal behavior (31). The subjects sits in a completely darkened room and, in a series of 20 trials, adjusts a luminous rod from a slanting to an upright position via a two-way switch, connected to an electric motor. The rod is enclosed by a luminous frame slanted in an opposite position to the frame. Throughout the trials the rod is placed 20° to the left and the frame 20° to the right of physical upright. Between the trials the light illuminating the rod and frame is switched off. Average field-dependence was determined on the mean deviation score on the 20 trials. A measure of the amount of change of deviation over trials (D) was defined as the mean deviation of the last 4 trials subtracted by the mean deviation of the first 4 trials (for a detailed description of the apparatus, see Andersson et al 1977) (1).

Interview. The interviews were semi-structured and aimed at covering patients' childhood conditions, relation to parents, and to other significant individuals, especially with respect to their more or less successful development towards emotional and social independence. Patients' motives for entering the program and their ability to discuss the postoperative adaptation in a realistic manner were assessed. Eating habits and physical activity were examined. The

material was scored in the following categories: civil status, childhood conditions, present situation, dependence, psychiatric history, aggressiveness, onset of obesity, present eating habits, physical activity, and attitude to surgery.

Other information. All patients were tested with Raven's Progressive Matrices and the Bender Gestalt Test to obtain information on perceptual-spatial ability and general intellectual capacity which, if deviant, might affect the performance on the main tests. No gross deviations from average performance were found in either tests.

Most of the patients were tested shortly before the operation on two separate days.

Clinical rating. Supplementary information was obtained by ratings made in collaboration with an experienced nurse who knew the patients well. Behaviour in the surgical ward was rated on a 5-point scale. The following variables were included: maturity, lability, aggressiveness, and ability to follow instructions. In addition, alcohol consumption and caloric intake were rated from the anamnestic interview.

Twenty-one patients participated in the psychological investigation. Administrative difficulties prevented all patients from taking part in the entire testing program (see below).

Statistical methods

Two-way analysis of variance (28) and the Spearman rank correlation test were used for evaluation of the differential weight loss. Differences between groups for metabolic and psychological variables were evaluated using Wilcoxon's rank order test and Fisher's exact test of 2×2 tables.

RESULTS

All patients were followed at least 18 months after the operation. The routine postoperative follow-up included a monthly visit for the first three months and a visit every three months thereafter. Gastroscoy and/or an upper G-I series has been performed on each patient at least on two occasions postoperatively.

Complications

Among our first six, two patients classified into groups B and C, respectively, (see below) had to be reoperated on and drained because of leakage from the upper pouch. Both had uneventful postoperative courses after the reoperation. One patient developed a deep iliac vein thrombosis which was surgically removed. Two accidental splenectomies were performed. One incisional hernia has been noticed.

Prolonged vomiting occurred in two patients in group A, which required short readmission to the hospital for intravenous fluids.

Weight loss

As mentioned earlier, patients were encouraged to reduce weight preoperatively: mean weight loss before surgery was 4.0 kg and the mean weight loss 18 months postoperatively was 34.4 kg. The average weight loss for the entire group after surgery is shown in Figure 1. Postoperative initial weight loss was rapid and at six months after the operation mean weight loss was 29 kg, most of which (23 kg) represented loss of body fat. The variation in weight loss was striking. Eighteen months postoperatively we found a mean weight loss of 30.4 kg with a range between 1-71 kg. Three of the patients started to regain weight six months after surgery and 18 months postoperatively they had almost reached their initial body weight.

The relationship between body weight reduction and body fat loss was similar in all patients; about 80 % of the weight loss could be accounted for by body fat. The grouping of the patients (see below), and the relationship between weight loss and other variables, yields identical results if weight loss is expressed as body weight reduction or body fat loss.

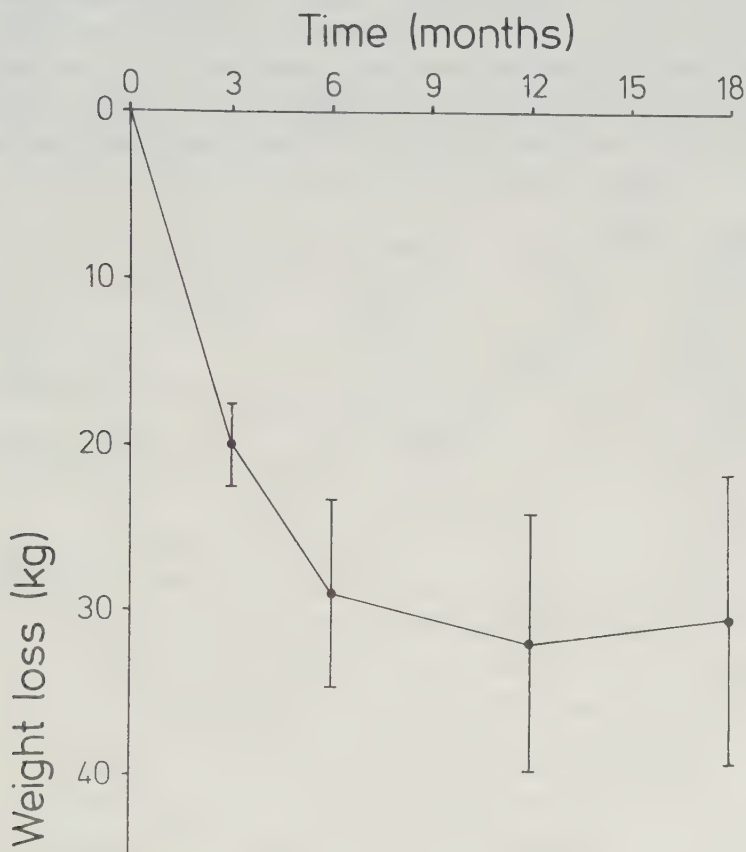


Fig 1. Body weight (mean $\pm$ SD) in 21 grossly obese subjects after gastroplasty operation. The initial weight, measured on the day before surgery, was 126 ± 21 kg.

Differential weight loss

The patients were divided into three groups, A, B, and C (Fig 2), which showed consistent differences in weight loss after surgery as confirmed by a significant time x groups interaction in a two-way ANOVA. Rank correlations computed on the entire group for weight at 6 and 12 months and 6 and 18 months, respectively, were highly significant ($r_s = .89$ and $.82$, $p < .001$), demonstrating that weight changes followed consistent patterns which were established already six months after surgery. The preoperative out-patient weight reduction (not shown in Fig 2) was equal in the three groups. Two of the four male patients belonged to group C and one to groups A and B, respectively.

Weight (kg)

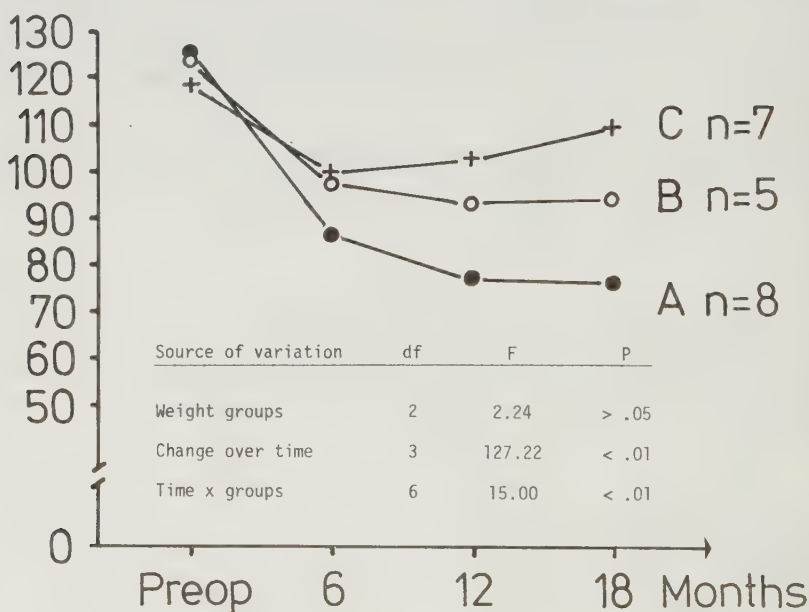


Fig 2. Differential developments of weight loss after gastropasty in three groups of patients. One patient, classified in the B group because of his pattern of weight loss (192, 163, 157 and 157 kg, respectively) has been excluded from this figure on account of his exceptional size.

Morphological and clinical variables in relation to weight loss

There were no significant differences between groups A, B and C with regard to initial body weight, body fat or lean body mass. Adipocyte size was similar in all groups (Table I). The age (Table I) was higher in the successful patients ($p < 0.001$ for group A compared to the groups B and C).

Table I.

Clinical and morphological data for patient groups A, B and C (see text). Data are given as mean $\pm$ S.D.

	A (n=8)	B (n=5)	C (n=7)
Age at operation (years)	38.4 $\pm$ 3.5	30.4 $\pm$ 7.8	29.6 $\pm$ 6.1
BW (kg)	125.6 $\pm$ 14.8	124.6 $\pm$ 8.0	118.7 $\pm$ 19.5
LBM (kg)	57.5 $\pm$ 9.1	55.3 $\pm$ 5.0	55.6 $\pm$ 12.3
Adipocyte size (μ m)	119.0 $\pm$ 8.9	120 $\pm$ 7.28	116.3 $\pm$ 8.55

As mentioned earlier all operations were performed by the same surgical team with rather little previous experience from gastric procedures for gross obesity. However, no difference (Table II) could be found between the groups A, B and C regarding the time of operation, i.e. the successful patients in group A were not operated upon as the last in the series. However, a higher rate of peroperative surgical complications occurred among the patients operated upon early in the series. No correlation between the surgeons' general judgement on the operation (see above) and the postoperative weight loss of the patients could be found.

The frequency of channel dilation (staple line rupture) or dilation of the upper gastric pouch as demonstrated by gastroscopy and/or upper G-I series in the three different groups are shown in Table II. Most of the channel dilations were discovered at the second check-up about 12 months after the operation and the patients could often tell at what time they had been able to eat without restrictions.

Table II.

Distribution of late postoperative complications and average position in operation series in group A, B and C (see text).

	A (n=8)	B (n=5)	C (n=7)
Average position in operation series	11.3	9.0	10.4
Enlarged channel	2	2 (+1?)	7
Enlarged pouch	2	1	-
Two applications of TA 90	3	1	1

Two applications of the T A 90 instrument were performed in three patients in group A, but only in one patient in groups B and C, respectively (Table II). Channel dilation occurred in three of these five patients and in eight patients of the 16 receiving only a single staple application.

Metabolic variables in relation to weight loss

The metabolic and biochemical variables in the three groups are shown in Table III. Variables reflecting thyroid function and adipocyte heat production did not differ between groups. Similarly, measurements reflecting glucose metabolism showed no consistent pattern between groups. No correlation between change in body weight and preoperative

plasma insulin level was found. The high mean values in groups A and C with respect to plasma insulin are explained by the presence of one or two subjects with extreme fasting hyperinsulinemia in these groups and the individual measurements showed an extreme inter-individual variation indicating that these data cannot be used, in the individual case, to assess suitability for operation.

Table III.

Biochemical variables in group A, B and C (see text). Data are given as mean +S.D.

	A	B	C
S-T4 (nmol/l)	139 <u>±</u> 24	140 <u>±</u> 30	132 <u>±</u> 19
S-T3 (nmol/l)	1.93 <u>±</u> 0.44	2.18 <u>±</u> 0.25	2.22 <u>±</u> 0.46
S-TBPM (arbitrary units)	0.95 <u>±</u> 0.17	0.89 <u>±</u> 0.05	0.96 <u>±</u> 0.06
S-rT3 (nmol/l)	0.24 <u>±</u> 0.05	0.30 <u>±</u> 0.06	0.25 <u>±</u> 0.09
B-glucose (mmol/l)	7.4 <u>±</u> 3.0	5.0 <u>±</u> 1.3	5.6 <u>±</u> 0.9
P-insulin (nmol/l)	26.3 <u>±</u> 20.7	5.5 <u>±</u> 4.5	21.2 <u>±</u> 14.8
P-glucagon (nmol/l)	163.4 <u>±</u> 146.3	140.8 <u>±</u> 24.8	231.4 <u>±</u> 53.6
P-triglyceride (mmol/l)	2.35 <u>±</u> 1.57	1.92 <u>±</u> 1.21	1.60 <u>±</u> 0.84
P-cholesterol (mmol/l)	6.30 <u>±</u> 1.46	5.07 <u>±</u> 0.41	5.28 <u>±</u> 0.87
P-HDL cholesterol (mmol/l)	0.92 <u>±</u> 0.12	1.13 <u>±</u> 0.29	0.87 <u>±</u> 0.16
P-LDL cholesterol (mmol/l)	3.95 <u>±</u> 1.39	3.26 <u>±</u> 0.47	3.65 <u>±</u> 0.68
Adipocyte heat production (pW/cell)	65.9 <u>±</u> 48.5	75.5 <u>±</u> 36.3	74.6 <u>±</u> 31.1
LPL activity in postheparin plasma (mU/ml)	66.8 <u>±</u> 30.7	58.0 <u>±</u> 16.1	75.8 <u>±</u> 32.2
HL activity (mU/ml)	469.1 <u>±</u> 125.8	411.7 <u>±</u> 141.3	591.2 <u>±</u> 259.4

With regard to lipid metabolism, there was a tendency towards higher P-triglyceride values in group A, but this difference did not reach statistical significance. The correlation coefficient between S-triglyceride concentrations and body weight reduction was 0.40 ($0.10 > p < 0.05$). Also the values of P-cholesterol, P-HDL-cholesterol and P-LDL-cholesterol did not differ between the groups.

Psychological variables in relation to weight loss

MCT test. Fourteen patients had been tested with the MCT before the operation. As more fully described elsewhere (19), the obese group differed from normal groups by showing more signs of an immature sense of self and signs of anxiety and by using regressive defenses, i.e. coping strategies which are normally abandoned during childhood. Contrary to our expectations, these features, which indicate a hampered ability to cope with stressful events in a mature way, did not differentiate the groups (Table IV). However, the few signs of sensitivity which were scored turned out to be ominous since they were found exclusively in group C.

Table IV.

The distribution of signs per person in MCT in the three weight groups A, B and C before surgery (see text).

Signs or combination of signs in MCT	Weight group				A + B	C
	A (n=6)	B (n=3)	C (n=5)			
a. regressive defence	2	0	0	a - c	8	1
b. regr. def. + anxiety	1	1	1	d - h	1	4
c. regr. def. + anxiety + repression	2	2	0			
d. sensitivity	0	0	1			
e. regr. def. + anxiety + sensitivity	0	0	1			
f. regr. def. + anxiety + repr. + sensitivity	0	0	1			
g. regr. def. + repr. + sensitivity	1	0	0			
h. depression	0	0	1			

p = 0.05 (Fisher's exact test)

Rod-and-Frame Test. In this test, the most successful patients were the most field-dependent as revealed by a comparison of group A with groups B and C. Group A was on the average more influenced by the frame or had a higher D-value, i.e. their performance deteriorated successively throughout the trial-sequence ($x \geq 10^0$ or $D \geq 4.0:A/B$, $p \sim .06$; $A + B + C$, $p = .05$, Fisher's exact test).

The clinical interview. Taken together, two variables, sensitivity and social phobia, by themselves differentiated group C from groups A + B ($p = .02$). Two groups of variables tended to be primarily associated with groups A or B and group C, respectively (Table V).

Table V.

The distribution of scores or combination of scores per person on variables in the clinical interview in subgroups A, B, and C. I and II denote variables that are positively related to the A-B, and C groups, respectively.

- I. Supportive social situation (1), concerned about appearance (2), recognizes apprehension concerning the operation (3).
- II. Previous anxiety reactions (4), sensitivity and/or social phobia (5), avoids talking about, belittles or believes to be "reborn" through the operation (6).

	A (n=7)	B (n=6)	C (n=6)
a. I	4	1	0
b. I+6	2	1	1
c. I+4	1	2	0
d. I+4+6	0	1	0
e. II	0	1	2
f. II+1	0	0	1
g. II+3	0	0	1
h. II+1+3	0	0	1

	A + B	C
a - d	12	1
e - h	1	5

$p = 0.01$ (Fisher's exact test)

We interpret variables (3) "recognizes apprehension concerning operation" and (6) "avoids talking about, belittles or believes to be reborn through operation", and possibly variable (2) "concerned about appearance", as indicating the absence (3, 2) and presence (6), respectively, of denial. The higher incidence of "previous anxiety reactions" (4) and "sensitivity and/or social phobia (5) in the C group as compared to the A and B groups, has a parallel in the distribution of signs of sensitivity in the MCT test (cf Table 4).

Clinical preoperative ratings. An estimated alcohol consumption above average ($n = 2$), in combination with immaturity (4-5) as evidenced by the patients' behaviour in the hospital, characterized four out of six patients in the C group but only one out of 13 patients in the A and B groups (Table VI).

Table VI.

The distribution of alcohol abuse and immaturity, as clinically rated, in subgroups A, B and C.

Clinical variables	Weight groups		
	A (n=8)	B (n=6)	C (n=6)
a immaturity only	3	2	1
b. alcohol overconsumption	1	0	1
c. a + b	1	0	4
d. neither a nor b	3	4	0
	A + B	C	
a + d	12	1	
b + c	2	5	

$p = 0.02$ (Fisher's exact test)

DISCUSSION

Treatment of obese subjects is a demanding task and requires a long-term commitment from the patient as well as from the doctor. There is growing consent that overweight as such is not a major indication for institution of a treatment programme, but that therapy should aim primarily at eliminating complications of a practical-clinical nature such as orthopedical problems and hypertension, and at eliminating psychological and metabolic complications which arise as a consequence of obesity. A careful clinical, psychological and metabolic evaluation is therefore necessary to select patients who will benefit most from treatment.

With all types of conservative or surgical therapy programmes there are wide inter-individual variations in the results of treatment, both with regard to weight loss and to improvement of psychological and metabolic aberrations (25, 26). It is therefore important to find means to predict, in the individual patient, the final outcome of various treatment programmes in order to make selection of the ideal therapy easier and to set a realistic goal for treatment. Certain morphological and metabolic variables have been shown to be correlated to subsequent weight loss during short-term caloric restriction (26), and adipose tissue cellularity seems to be of importance for the long-term results of conservative treatment (13).

Thus, the initial body weight, thyroid hormone status and resting metabolic rate have been shown to predict as much as 75 % of the inter-individual variation in short-term weight loss during fasting (26). Also, it is well established that patients with hyperplastic obesity lose weight more slowly, but retain a reduced body weight for longer than patients with hypertrophic obesity during conservative treatment (13). Our results demonstrate that these variables have little predictive value for the results of gastroplasty. Similarly, the other metabolic variables tested, reflecting glucose metabolism,

lipid transport and adipose tissue metabolism - all of which are frequently abnormal in obesity - were not related to weight loss after surgery.

As is the case with any surgical procedure, the technical outcome of the gastroplasty operation may be of great importance for the long-term result. However, we found no relation between the surgeons immediate judgment on technical difficulties of the operation and final result, nor was there accumulation of patients with little weight reduction early in the operation series.

Many failures may be explained by late surgical complications, such as enlargement of the pouch, staple line rupture leading to dilation of the channel which allow larger daily food intake than the typical 500-800 kcal and thereby affect the long-term results. As a matter of fact, all patients in group C developed channel dilation, which seems necessary for weight maintenance after operation. We could find no peroperative surgical explanation for the accumulation of channel dilations in this group. The use of one or two applications of the TA-90 instrument, in order to prevent staple line rupture and channel dilation, has been much discussed (9). As seen in Table II, two applications were performed mainly in the A group, but channel dilation was equally frequent among patients with one or two applications. Four (possibly five) cases of channel dilation and three cases of enlarged pouches were found in the A and B groups. These patients lost weight successfully despite late postoperative complications. Apparently they were able to adhere to a restricted diet, perhaps due to the satisfaction felt after the initial weight loss. This finding suggests that psychological factors are important for succesful weight loss in groups A and B. Similarly, we suggest that psychological factors (see below) might be of relevance for the bad results in group C. Thus it is possible that the accumulation of late complications in group C represents an inability of these patients to comply with the postoperative regimen, and that the

channel dilations result from staple rupture due to excessive feeding. This interpretation is consonant with the finding that at least 40 % of those patients who are admitted for revision remain failures even after a second operation (9).

The psychological features differentiating the patients in the C group from those in the A and B groups seem to form a coherent pattern. We would stress, in particular, the combined signs of immaturity and sensitivity. Anamnestic data on the patients in group C point to a higher incidence of above average alcohol consumption and social phobia and/or sensitivity. In the clinical interview, which was made when the patients were facing the operation, they expressed less realistic expectations and did not recognize an adequate apprehension, signs of an immature denial of reality. Signs of sensitivity characterized their MCT protocols. This feature which implies a disposition to respond to marginal external as well as internal cues, is often accompanied by an increased anxiety and involves a heightened psychic vulnerability (22). Sensitive individuals often find it difficult to defend themselves against the anxiety they are liable to experience. It seems reasonable to assume that, for our sensitive patients, food and the act of eating serve anxiety-curbing purposes. Since a sensitive disposition heightens an individual's vulnerability to criticism, the more or less openly expressed contempt and condescension that obese individuals often encounter can be expected particularly to affect patients in group C, an interference which agrees with the higher incidence of social phobia in this group. The use of alcohol and food as sedatives lies near at hand. In support of this reasoning, one patient in the C group ate large quantities of maionnaise directly from tubes; another patient in this group regularly woke at night and had fried food in combination with alcoholic liquors. Finally, the significantly lower mean age of these patients is consonant with the more frequent signs of immature responses. A sensitive disposition can be expected to give rise to

more anxiety in young adulthood than later on when familial and social conditions stabilize.

The challenging finding that the most successful patients, those in group A, were the most field-dependent, as measured by RFT, may indicate that a factor of some significance for the patients' post-operative adaptation is their mode of associating emotional and physical aspects of weight loss. Field-dependent individuals tend to have a low introspective self-awareness (11) and are thus less inclined to perceive situations in terms of their private significance - endow them with "meaning". Instead they rely more on information and interpretations supplied by those around them (30). This may make them psychologically less vulnerable during rehabilitation, since they would not attribute unwarranted emotional significance to changes following the operation such as the restricted food intake or somatic side effects like vomiting. On the other hand, they are more dependent on a stable and supportive social environment. This argument is supported by a poor outcome for the sensitive patients who are characterized by the opposite orientation (22), and by the finding that patients in the A group tended to live in a stable and supportive social environment.

The small sizes of the subgroups showing differences in weight loss after gastroplasty may make conclusions regarding the predictive value of specific variables hazardous. Correlations, although statistically significant, may be accidental. On the other hand, the clinical value of predictive factors is very limited when a great number of patients are required in order to receive statistically significant results. Given these limitations, the usefulness of small materials may be considerable if the results obtained are coherent and interpretable.

In contrast to short-term dietary treatment, like a supervised period of fasting, surgical treatment of obesity is not completed at the operation table. After surgery the patient, now in her habitual

environment and on a long-term basis, has to adopt radically new food habits. The patient's ability to adapt herself to a major change in her life is decisive for the outcome of this process of adaptation. Accordingly, the present study shows that the technical outcome of the operation is not crucial for all patients for the weight loss obtained; also, metabolic and morphological differences between patients that affect weight loss when food intake is controlled are less influential than psychological characteristics that determine the patients' adaptive capacity. The psychological profiles of these patients have been assessed with rather sophisticated experimental techniques. However, it is likely that in clinical practice similar information can be obtained by less cumbersome methods, such as a structured interview by a trained physician with special emphasis to signs of immaturity and sensitivity.

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